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CONTENTS.

PAGE.

An Analysis of the Cases of Tabes in the Johns Hopkins Hospital and Dispensary from its opening in May, 1889, to December 1, 1898. By H. M. Thomas, M. D., - - - - - - - - - - 51

On Typhoid Septicæmia, with the Report of Two Cases, one of which was a Typhoid Infection without Intestinal Lesions. By August Jerome Lartigau, M. D., - - - - - - - - - 55

Cavities in the Brain Produced by the Bacillus Aerogenes Capsulatus. By Robert Reuling, M. D., and Arthur P. Herring, M. D., - - - - - - - - - - - - - - - - - 62

Acute Fibrino-purulent Cerebro-spinal Meningitis, Ependymitis, Abscesses of the Cerebrum, Gas-Cysts of the Cerebrum, Cerebro-spinal Exudation, and of the Liver, due to the Bacillus Aerogenes Capsulatus. By W. T. Howard, Jr., M. D., - 66

Proceedings of Societies:

Hospital Medical Society, - - - - - - - - - - - - - - - 69

Resistance to Quinine of Certain Forms of Malaria [Dr. Camac];—A New Method of Staining Malarial Parasites [Dr. Futcher];—Laparotomy for Intestinal Perforation in Typhoid Fever [Dr. Thayer];—Presentation of Pathological Specimens [Drs. MacCallum and Harris.]

Notes on New Books, - - - - - - - - - - - - - - - - - - 72

Books Received, - 74

AN ANALYSIS OF THE CASES OF TABES IN THE JOHNS HOPKINS HOSPITAL AND DISPENSARY FROM ITS OPENING IN MAY, 1889, TO DECEMBER 1, 1898.

By H. M. Thomas, M. D., *Clinical Professor of Nervous Diseases, Johns Hopkins University, Neurologist to the Johns Hopkins Hospital.*

In the records of the Dispensary of the Johns Hopkins Hospital there are one hundred histories which have been classed as tabes. Of these I have excluded eight histories, either because the records are too incomplete, or because the diagnosis seems to have been a mistaken one. Twenty-seven cases have been treated in the wards of the Hospital, but unfortunately for the purposes of this paper, many of them were private patients in whose histories the records are often not complete.

Eight (8) of the patients were treated both in the wards of the Hospital and in the dispensary, and we therefore have for comparison the histories of 111 cases of tabes. That these histories are not all equally good, need not be said, and, indeed, not a few of them leave much to be desired.*

Race.—White, 106; negroes, 5. Of the 106 white patients 70 were born in this country, 17 were Germans, 6 were Irish, and England, Scotland and France were each represented by 2; 6 patients were simply registered as white.

The small number of negroes is of particular interest, and deserves more detailed attention. We have, as I have just said, seen but five colored patients, in whom the diagnosis of tabes seemed in the least justifiable; that is to say, but 4.5 per cent. of our cases of tabes have any discoverable African blood in their veins, for it is to be remembered that in the eye of the law and of the statistician it takes but very little African blood to make a negro.

In the two years ending November 1, 1898, there were registered in the dispensary 35,796 new cases. Of these 3598 were negroes. This makes the negroes represent a little more than 10 per cent. (10.05 per cent.) of the new cases treated. In the cases of tabes, however, our percentage of negroes is only 4.5, which is less than half what it should be if the negroes were represented in their proper proportion. This difference, although interesting in itself, is hardly great enough to warrant

*After having read through some 130 histories, I feel that I might with propriety make some observations upon the taking of histories, which, if followed, would be useful at least to the one who has to tabulate them, but I shall not, only saying as I pass, that it is a subject which deserves more attention than is often given to it.

much attention were it not for other considerations. I think I shall not be accused of exaggeration when I state that the great majority of physicians who are qualified to judge have come to the belief that syphilis is the chief, if not the only, cause of tabes.

We in the South know that syphilis is a very common disease among the negroes, but upon examining the records of the dispensary, I was surprised to discover how common it is. In the two years selected for comparison there were treated in the Genito-Urinary and Skin Departments 228 men who were suffering either from the primary syphilitic sore or the secondary skin eruptions. Sixty-three of these men were negroes, that is 27.63 per cent. of the whole number. When we compare this percentage with that which the negro men represent in the whole number of the men registered in the dispensary, during these years, is quite startling. There were registered 17,888 white males and 1223 colored males, *i. e.* 6.39 per cent. of colored males. Unfortunately there are included in this males of all ages, and so the comparison is not perfectly fair; but I believe the error is not great. We have then, during these two years, the negro males, representing 6.39 per cent. of all the males treated in the dispensary, but of the cases of syphilis seen in men during this time, the negroes make up 27.63 per cent.

If we determine the percentage which the cases of syphilis in white and black men, treated in the Skin and Genito-Urinary Departments during two years, bears to the whole number of males of each color admitted to the dispensary during that time, we find it is for the whites 0.91 per cent. while for the negroes it is 5.15 per cent. From this it would seem that in the men coming to this dispensary, the percentage of early syphilis is more than five and a half times greater in the negro race than it is in the white.

Sex.—Men, 92 white, 5 colored—97; women, 14 white—14. That is, the women represented about 12.6 per cent. of the whole number. In the dispensary the percentage of women suffering from tabes is smaller, being a little more than 9 per cent. (9.17 per cent.), whereas female patients represent a little more than 46 per cent. of all patients in the dispensary. In the cases of tabes treated in the wards of the Hospital, the percentage of women is distinctly larger than in the dispensary, reaching 25 per cent.

It is interesting to note that in the first 50 cases treated in the dispensary there was but one woman, and that she was the 50th case. On the other hand, in the wards, 3 out of the first 5 cases were women. This shows how very unreliable such statistics are unless a very large number of cases is considered.

Five of the patients were seen in the private wards of the Hospital and were from the higher strata of society. This is contrary to the usual statement that tabes affects women of the lower classes far more frequently than those who are more fortunately situated. Moebius, out of 40 cases, found only one belonging to the upper classes.

This relative immunity that women appear to enjoy from tabes cannot be due altogether, I believe, to the fact that fewer women suffer from syphilis than men. That syphilis is more common among men seems to be universally believed, and I have no doubt is true as a general proposition.

In certain classes of society, however, the difference, if it exists at all, cannot be great. As an illustration of this, the records of the Skin Department are instructive. During the two years preceding November, 1898, 130 men and 121 women were treated for the skin manifestations of syphilis, but during this time, more men were admitted to the dispensary in general, as well as to the skin clinics, so that if these figures indicated anything as to the liability of syphilis, it would seem that women are slightly more liable to the disease than men. We have as yet seen no case of tabes in a negro woman,* whereas syphilis is most common in them; 42 of the 121 cases of skin syphilis in women were negresses, *i. e.* 34.87 per cent. The percentage of black females to the whole number of females in the dispensary is 14.23 per cent.

Age of Onset.	No.
25–29	8
30–34	17
35–39	24
40–44	27
45–50	16
50 and over.	15
Total,	107

The time of onset of the disease showed nothing of very great interest. Most of the cases developed between 30 and 50. The youngest case was 25, and the oldest 66. The series includes 15 cases which developed after 50, and this is a larger number than would be expected. It may be doubted whether these senile cases should be included, but I do not see how we can do otherwise when the patients present the symptoms and signs that would have led to the diagnosis of tabes had they occurred at an earlier age.†

The onset of tabes is often very insidious and the early stages may last for many years and it seems probable that some of these patients may have been unconscious or may have forgotten the first symptoms.

Duration of the Disease at the Time of Examination.—Cases, 104. This could be determined with more or less accuracy in 104 cases. Duration 1 year or less, 18 cases; between 1 and three years, 34 cases; between 3 and 5 years,

* Since this analysis was made we have examined a colored woman in the Neurological Dispensary (No. 9525) who is suffering from symptoms that indicate tabes; irregular pains, numbness of the feet, difficulty in walking, loss of knee kicks, objective sensory disturbances on legs. The pupils were normal, and no history of syphilis could be obtained.

† Neurol. No. 2947. A man 70 years old, who gave the history of having had a venereal sore at 25, which was followed by a doubtful secondary skin eruption, came to the dispensary complaining that for the last 4 years he had had difficulty in walking in the dark. He had also had slight shooting pains and his feet felt numb. His pupils were of normal size. They reacted very slightly to light, the left better than the right. Both pupils reacted well during accommodation. His knee jerks were absent, his walk was stamping, the heel being brought down first, and he was unable to stand firmly with eyes closed. There was considerable anæsthesia of his legs.

17 cases; between 5 and 10 years, 24 cases; between 10 and 20 years, 10 cases; 30 years, 1 case.

Most of the cases (69) were seen during the first 5 years of the disease, but in 11 cases it had lasted 10 years or more, once even reaching 30 years.

Etiology.—Believing as we do that syphilis is the cause of the vast majority of cases of tabes, we have practically confined our attention to this factor.

Only men have been considered in the following table, and there are definite notes in 95 of the 97 cases.

Exposure to venereal contagion denied... 3			
Exposure admitted but infection denied.. 7			
Infection denied (exposure?) 7			
Venereal infection denied.....	17	17.89	per cent.
Gonorrhœa alone.. 18			
Venereal sore denied.....	35	36.84	"
Gonorrhœa with chancre—indefinite. ...15			
Gonorrhœa with syphilis 20			
Gonorrhœa*	53	55.78	"
Chancre, syphilis.....38			
Syphilis with no history of chancre..... 2			
Certain syphilis.....	40	42.1	"
Chancre indefinite..... 20			
Possible syphilis.....	60	63.1	"

By certain syphilis is meant the definite history of a chancre which was believed to be syphilitic and was treated as such, or the history of a chancre which was followed by secondary manifestations, and in two instances, where skin eruptions were recognized as syphilitic, although there was no history of the primary sore. All other venereal sores have been tabulated as indefinite chancres.

In taking the histories, the supposition has been that in all cases of tabes syphilis has preceded, and the burden of proof has been with the patient who denied its presence.

The results are: Certain syphilis, 42.1 per cent.; possible or probable syphilis, 63.1 per cent. These figures fall below those obtained by many of the later observers, but it is not due to lack of zeal.

Some time ago I analyzed the sexual histories of 1238 men who came to the Neurological Dispensary suffering from all sorts of troubles; in them I found certain syphilis in 10.9 per cent., and possible or probable syphilis in 21.4 per cent.

These percentages are much smaller than those found in tabes and the inference that syphilis bears an important relation to the development of tabes is plain, but I must resist the temptation of entering fully into the discussion of syphilis as the cause of tabes. It may not be, however, out of order to sum up what the cases studied here seem to show:

1. In a large proportion of cases of tabes, a history of syphilis can be obtained.

2. In a certain and not inconsiderable number of cases there is no history of a venereal sore or other syphilitic manifestations.

3. In negroes, tabes is relatively uncommon, whereas syphilis is much more common in them than in the white population.

4. The partial immunity of women is greater than can be satisfactorily accounted for by the relative infrequency of syphilis among them.

I do not take these conclusions as indicating that syphilis is not the most important cause of tabes; on the contrary, they seem to me to speak in favor of this belief. The fact that we were unable to elicit the history of syphilis in 36 per cent. of our cases does not of course prove that syphilis was not present in a large proportion of these cases.

Although tabes does not seem to be common in the negro, when it does occur, it has usually been preceded by syphilis. In four of our five cases there was the history of a venereal sore, and the same has been shown in the cases of tabes in women.*

That syphilis is not the only factor in this causation of tabes does seem to be shown. What the factors are that make white men so much more liable than black women to the development of tabes, I am sure I do not know; but of this I feel reasonably certain—that it is not due simply to the difference of primary syphilis among them. To say that it is due to a racial and sexual difference in the power of resistance of the nervous system, does little more than restate the facts.

Virchow† has lately raised his voice against the methods of study which have led to the all but universal belief that tabes is always directly dependent upon preceding syphilis.

The time between the syphilitic infection and the first symptoms of tabes varies a good deal. This point was determined in 47 cases.

Tabes developed after the venereal sore in 47 cases. In the first 5 years, 6 times; in the second 5 years, 10 times; in the third 5 years, 13 times; in the fourth 5 years, 10 times; in the fifth 5 years, 4 times; after 25 years, 4 times.

The shortest interval was 2 years, and the longest intervals were 26, 27, 30 and 42. It occurred about equally in the second, third and fourth five years.

As to the other causes of tabes, our histories show nothing important.

Initial Symptoms.—Either alone or associated, the following symptoms occurred as initial symptoms: Pain, 57 times; ataxia, 24 times; numbness, extremities, 6 times; eye symptoms, 20 times; nausea and vomiting (gastric crises), 4 times; paralysis of bladder, 5 times; loss of sexual power, 1 time; paralytic attacks, 2 times; mental symptoms, 1 time; neurasthenia, 1 time.

Pain.—Pain was the first symptom in the majority of cases, occurring first or very early in the disease 57 times. It was unassociated 41 times and accompanied by other symptoms 16 times.

Ataxia.—Difficulty in walking and ataxia were the first symptoms 15 times, and were associated with other symptoms 9 other times.

Eye symptoms.—Double vision was the initial symptom 6 times. Dimness of vision occurred first alone 4 times. Double vision and dimness of vision were associated once, and double

* Note.—In some of the early cases the history in regard to gonorrhœa was not particularly noted and for this reason the number given is probably too small.

* Kron. Deut. Zeitschr. f. Nervenheilk., XII—1898, p. 303. "Ueber tabes dorsalis beim Weiblichen Geschlecht."

† Centralb. f. Nervenheilkunde in Psychiat., Nr. 105, 1898, p. 625.

vision with other symptoms 7 times. Ptosis was the first symptom, associated with pain twice.

Numbness of extremities occurred alone 4 times, with pain twice.

Paralysis of the bladder occurred alone 4 times, with pain twice.

Subjective Sensory Symptoms—*Pain.*—In 71 cases pain was a prominent symptom. This was usually described as the characteristic lightning or shooting pain. In most cases it was severe, but in some it was mild. The pains were usually localized in the legs, but in three cases they were confined to the body, and in two to the arms, and in six others they were more or less general.

Girdle sense or pain, 27.—This symptom was noted as being present in 27 cases. Sense of numbness in the extremities, 45.

Numbness of the feet was complained of 30 times, the patients often describing a feeling as if the floor were not solid or as if they were walking on some soft substance. There was numbness in both the hands and feet 12 times, and in the hands alone 3 times.

Crisis.—Gastric crises, 9. There were nine patients who gave the history of having had gastric crises. In two of the cases the nausea and vomiting were unaccompanied by pain. In one of the cases very typical gastric crisis and Argyll-Robertson pupils were the only symptoms of tabes.

Laryngeal crises, 2. Two of our cases were subject to spasmodic cough; one of them was a typical case of tabes, but in the other the diagnosis was doubtful.

Rectal crisis, 1. One patient complained that early in his disease he had been subject to intense pain that began in the penis and ran to the rectum.*

Eye symptoms—Optic atrophy, 11.—Optic atrophy occurred in 11, possibly 12 cases. The twelfth case was one in which one optic nerve looked as if atrophy had begun. In the other cases it was double.

Eye muscle paralysis, 33.—Transient double vision was noted as having occurred in 20 cases, and in 13 other cases there was a noticeable weakness of one or more of the external muscles of the eyeballs. In one of these cases there was complete external ophthalmoplegia.

Ptosis was present in 7 cases, and in 1 there was nystagmus.

Pupils—Size.—The pupils were unequal in 30 cases. The left was larger than the right 18 times while the right was the larger 8 times. In four instances the history did not specify which was the larger.

There was contraction of the pupils in ten cases and they were noted as dilated twice.

Pupillary reflexes.— Argyll-Robertson pupils, 70. Both pupils immovable to light, reacted well during accommodation, 59. In one eye, 3. Reacted slightly to light, well to accommodation, 8.

The pupillary reflexes were said to be absent 8 times, and weak 3 times. They were found to be normal 21 times.

Ataxia.—Ataxia was present 91 times: in the legs alone, 78 times; in the arms alone, 2 times; in both arms and legs, 11 times. There was no ataxia 8 times.*

Romberg's symptom, 82.—Present 82 times, marked 59 times, slight 23 times, absent 7 times, not noted 22 times.

Ataxia with optic nerve atrophy.—In the cases which showed atrophy of the optic nerve, ataxia was marked in 2 cases. It was slight in 8 cases and was absent in 1. In two of the cases Romberg's symptom was marked in spite of the patients being blind. It was very slightly marked in 4 cases, and was absent in 4 and not noted in 1.

Deep reflexes.—The knee jerks were absent 87 times; weak 6 times; normal 4 times; not noted 14 times.

Bladder.—The condition of the bladder was noted in 83 cases: Weakness, 35 times; paralyzed, 19 times; normal, 29 times.

Sexual power.—The sexual power was inquired into in 75 cases: Power and desire lost, 38 cases (marked increase before the loss in 3 cases); power and desire weakened, 24 cases; power lost, desire retained, 1; power and desire increased 1; normal, 10; sexual power present, intercourse without sensation, 1 case.

Objective sensory disturbances.—There are definite notes in this respect in 90 cases: Objective sensory disturbances were present in 78 cases; absent in 12 cases.

These were more often in the legs (40 times), but were also demonstrated in the arms and about the chest.

Definite areas of anæsthesia were marked out about the chest in several cases, but this was looked for and not found in more cases. The number of examinations, however, was not sufficient to make the definite proportions of any great value.

Muscular sense.—There were definite notes in 44 cases. In these it was disturbed 38 times, normal 6 times.

Trophic disturbances— Charcot's joints (Arthropathies).—These occur in a typical manner in 5 cases. There was suspicious enlargement of the joint in 3 cases.† In the 5 cases it occurred 3 times in the knee joints, 1 in the shoulder, and 1 in the elbow.

Perforating ulcer.—This occurred 5 times.

Mental Symptoms.—There were mental symptoms present in seven cases, and in one case there was a history of a previous attack of acute insanity, and in one epilepsy had been present from the 14th year up to the time of the onset of tabes, at 44. Since then there had been no fits.

In the 7 cases showing mental symptoms general paresis was suggested. In two of the cases this disease developed while the patients were under observation.

* Since this list was completed I have seen another case of tabes that complained of the same symptom.

* In eight (8) of the cases the ataxia developed quickly. At times this followed an accident, but at other times there was no cause that could be determined. In most, if not all, of the cases, symptoms of tabes had been present for some time before the acute development of the ataxia.

† In one of these patients, who, since this was written, has returned to the dispensary after an absence of two years, and who had, at the time of his first examination, in 1897, a suspicious swelling of the last phalangeal joint of the left index finger, there has developed an undoubted tabetic arthropathy of the right thumb. This patient also had a healed perforating ulcer.

ON TYPHOID SEPTICÆMIA, WITH THE REPORT OF TWO CASES, ONE OF WHICH WAS A TYPHOID INFECTION WITHOUT INTESTINAL LESIONS.

By August Jerome Lartigau, M. D., *Assistant in Pathology and Bacteriology, Bender Hygienic Laboratory, Albany, New York.*

Our knowledge of the various forms of typhoid infections has rapidly increased within the past few years, and more particularly that regarding the character of those atypical and more rare forms, the chief interest of which lies in the singularity of localization of the typhoid bacillus. The value of the contributions of recent years is largely the outcome of improved bacteriological technique and closer and more accurate study of the natural history, cultural behavior and experimental manifestations of the bacillus typhosus and the bacillus coli communis. Investigators have appreciated more and more the necessity of exact methods of differentiation between bacterial forms, and especially between more or less closely allied species, such as the bacillus of typhoid fever and the colon bacillus.

The absence of precise methods of differentiation between these two micro-organisms by the earlier workers in this field has, of necessity, thrown much discredit upon the conclusions and results of otherwise much good and brilliant work. The belief of the passage into, and existence of, the typhoid bacillus in the blood of the general circulation is by no means a new one, as shown by the writings of some of the early writers who worked upon typhoid fever. Rütimeyer, Almquist, Meisels, Neuhaus, and others, claimed to have cultivated the bacillus from the general blood and that of the rose-spots during life, but their work, through the latter researches of Janowski, Stagnitta, Grawitz, Fraenkel and Simmonds, and Sittman has not received acceptance. According to some observers the typhoid bacillus in almost every case at some time of the disease escapes into the general circulation from the more common foci of infection.

This view has received some support from the investigations of late years, demonstrating the great multiplicity of localization of Eberth's bacillus in the human economy: lesions of the bones, pulmonary implications, uterine infection, abscesses of various nature, etc., in all of which the organism has been found in pure culture. Wright and Semple[1] and Sanarelli[2] and other observers regard typhoid fever as primarily a blood infection, the two former writers basing their contention largely upon the fact that in the urine of almost every case suffering from typhoid fever they were able to find the specific organism. Recent researches, however, show more and more conclusively that the typhoid bacillus is not, commonly, to be found in the blood of the general circulation. The explanation of this apparent discrepancy between the results of Sanarelli, and Wright and Semple and other observers, who from their investigations have shown that the bacillus is only infrequently found in the general circulation, is to be found probably in the suggestive experiments of Wyssokowitsch[3] and the observations of Welch and Nuttal[4]. The first experimenter in some very interesting experiments upon rabbits was able to show that the organs in which typhoid bacilli are commonly found play a very important rôle in the removal of introduced bacteria from the blood. After injecting pure cultures of the typhoid bacillus into the blood the animals were sacrificed at the end of eighteen hours, and bacteriological examination invariably failed to show bacilli in the blood of the general circulation, but always showed them in great numbers in the spleen. Welch and Nuttal in 1891, on the other hand, demonstrated the bactericidal properties of human blood serum for the typhoid bacillus, an observation since confirmed by a host of investigators.

Instances of typhoid septicæmia diagnosticated during life by isolating the bacilli from the blood are very scanty in number. Bozzolo,[5] Guarnieri,[6] and Silvestrini[7] have reported cases of this nature; Wiltschour[8] in the examinations of 35 cases found it once; Ettlinger[9] similarly succeeded in cultivating it from the blood during life, but a second culture in the same case from the vein of the forearm, the day before the patient's death, gave a doubtful result. Thiemich[10] found it once in the blood taken during life from a vein of the forearm, and Stern[11] was likewise successful in two instances. P. Teissier[12] isolated the typhoid bacillus from the blood of a young man in the 15th day of his disease; Kühnau[13] grew the organism from the blood of a pregnant woman during life in which the subsequent post-mortem findings confirmed the existence of a typhoid septicæmia; more recently this writer[14] has published the reports of nine additional instances in which he found typhoid bacilli in the blood out of 41 cases of typhoid fever submitted to bacteriological examinations. E. Bates Block[15] has reported a very conclusive example of this kind in which the typhoid bacillus was discovered in the blood during life on two different occasions, at an interval of four days. This case presents several interesting features, among others being the fact that a culture taken on the day before the patient's death contained the bacillus typhosus, whilst the bacteriological examination, post mortem, demonstrated its presence only in the spleen, liver, placenta, and kidneys, and the bacillus pyocyaneus in the heart's blood. In the recent Medical and Surgical Reports of the Presbyterian Hospital,[16] Walter R. James and George A. Tuttle report three cases in which they succeeded in isolating the bacilli from the blood during life.

The diagnosis on the autopsy table of general invasion by the bacillus typhosus is far less rare than its recognition during life, but it must not be supposed that as a post-mortem finding it is a frequent occurrence. The very early reports of this kind will not be considered in this paper, since their study was carried on at a time when the differences between the typhoid bacillus and the colon group were less appreciated than now. Karlinski,[17] Vincent,[18] Klein,[19] Banti,[20] Wright and Stokes,[21] Flexner,[22] Carter,[23] Chiari and Kraus,[24] and finally Blumer[25] have contributed a fair number of instances in adults that showed the organism in the blood after death. Typhoid septicæmia is an occurrence of comparatively greater frequency in the fœtus born of a mother suffering from typhoid infection. The passage of the organism from mother to fœtus has repeatedly received demonstration in the observations of

Frascani[26], Janiszewski[27], Freund and Levy[28], Dürck[29], Etienne[30], Marfan[31] and probably earlier observers.

The question of the bacterial associations in this class of infections is an exceedingly interesting one, and especially the influence of secondary infections in modifying the relation of the patient to the typhoid bacillus. Vincent[32] in 1891 called attention to the importance of the streptococcus in typhoidal infections. This observer found in cases of typhoid fever brought to autopsy the streptococcus and typhoid bacillus associated in six out of thirty-one cases. The investigations of Flexner[33] similarly demonstrated the frequency with which the streptococcus is found as a complicating factor in this disease; other observations of the same nature were made by Wright and Stokes[34], Netter[35], E. Fraenkel[36], Karlinski[37], Carter[38], and others.

The recently published case by Blumer[39] deserves special mention, not only as an instance of typhoid and streptococcus septicæmia, but also as a rare example of combined typhoid and streptococcus puerperal infection. The case was that of a married woman, 34 years of age, who was confined by a midwife. On the sixth day of the puerperium the patient, shortly after a hearty meal, was taken with dyspnœa and incoherency of speech. She rapidly became delirious and semi-comatose. The temperature was 100.8 F. The uterus was apparently normal. Patient died two days after the onset of her trouble. The post-mortem examination showed the existence of typhoid fever: swelling and ulceration of Peyer's patches in the lower end of the ileum, acute spleen tumor and enlargement of mesenteric glands. The cultures from the heart's blood, liver, spleen, and uterine cavity, contained the streptococcus pyogenes and the bacillus of typhoid fever.

For the abstracts from the histories of the two following cases I am indebted to Drs. Henry Hun and Joseph D. Craig, of Albany, New York:

Case I.—Miss A., 20 years of age, came under observation October 19, 1897, complaining of gastric disturbances and fever.

The past history is unimportant, except that three years before she had an attack of grippe, which was accompanied by very irregular and alarming heart action. On the 16th day of October, 1897, the patient was taken ill with nausea, and was actively sick at her stomach. The following day she still felt ill and a physician, who was called in, found a temperature of 102° F., together with a very decided degree of prostration. The patient brought under observation at this time did not show any tenderness or gurgling in the right iliac fossa and there had been no diarrhœa. From this time there was fever varying from 102° F. to 106.6° F.—the temperature at the time of her death. The spleen and liver became enlarged, later delirium supervened, vomiting persisted and cardiac weakness became prominent; no diarrhœa at any time. Patient died October 25, 1897.

The autopsy was made on October 26th, 15½ hours after death.

The following notes are abstracted from the autopsy protocol:

Exterior.—Body of a slender-built, moderately well-nourished girl. Rigor mortis well marked all over. Post-mortem lividity in the dependent parts. Pupils mid-wide and equal. Mucous membranes slightly cyanotic. Surfaces of body generally pale, subcutaneous fat moderate in amount. Abdominal muscles of a homogeneous red-brown color. Peritoneal cavity dry, parietal layer smooth; visceral layer shows numerous areas over which there is congestion apparently corresponding to Peyer's patches. Omentum delicate, free from adhesions, completely covering the intestines. Appendix about 9 cm. long, has a distinct mesentery to within 1 cm. of its tip; passes downward and inward across pelvic brim. The liver is visible two fingers' breadth below the costal margin in the mammary line. Spleen not visible. Both pleural cavities were dry; both lungs presented about the same appearance; the upper lobes were slightly congested; the lower and middle lobes on the right side and the lower lobe on the left were much congested, and on pressure a large quantity of dark blood could be expressed. A small quantity of mucus could be expressed from the medium-sized bronchi. Bronchial mucous membrane irregularly congested.

Heart.—Pericardium contains no excess of fluid. Pericardium is smooth. There are a few pin-point sub-pericardial hemorrhages. Heart contains fluid blood. The endocardium on the right side is smooth, the muscle shining through it has a somewhat mottled appearance in places. The tricuspid and pulmonary semilunar valves are normal. The length of the right ventricle is 6 cm.; the average thickness of the wall 4 mm. The pulmonary artery has a circumference of 5 cm. The endocardium of the left side of the heart is, in places, slightly thickened over the auricle. The ventricle is normal. Aortic and mitral valves are normal. Heart muscle is rather flabby and on section has a very cloudy, grayish-brown color, in places somewhat mottled in appearance. In both coronary arteries, which are patent, are small elevated areas of fatty atheroma. Spleen is much enlarged, measuring 17 x 20 x 5 cm. The capsule is smooth, tense; consistency of organ much softer than normal. On section the organ is of a chocolate-red color. The pulp is considerably increased in amount. The Malpighian bodies are plainly visible as pin-point, gray, circular areas. Liver is considerably increased in size, measures 23x19x6½ cm. There seem to be a number of pinhead-sized hemorrhages beneath the capsule; consistency much softer than normal. On section the organ has the typical boiled appearance; the lobules are indistinct, the peripheries being quite yellow where they can be made out. Scattered throughout the organ is a number of pinhead-sized blood-red areas, apparently hemorrhages.

The adrenal glands appear normal.

Kidneys of about the same size, averaging 13 x 4½ x 3 cm. fibrous capsule normal and strips off easily; surface smooth; surface veins little dilated. On section cortex is swollen; cortex markings are somewhat indistinct; the glomeruli barely visible; the medulla congested. Pelvis appears normal.

Stomach and pancreas and female generative organs not examined.

Intestines.—Duodenum slightly bile-stained. Mucous membrane slightly congested; jejunum shows similar changes, but with apparently no ulcerations. In the ileum, beginning 80 cm. above the iliocæcal valve, are a series of lesions affecting the solitary follicles and Peyer's patches. They are least marked in the upper portion of the ileum, where they consist in a great swelling of the lymphatic apparatus. The solitary follicles

measure as much as one-half cm. in diameter. The most recent swollen patches are considerably elevated above the surface. They have a mottled appearance, the predominating color being pink, and the mottling being due to yellowish areas, presumably of necrosis, as in one or two places the surface has been broken and ulcers formed. In the lower portion of the ileum the swelling is much more extensive and the necrosis much more marked. The solitary follicles are often the size of a large pea, their inner surface being capped with an ulcerated area on which a yellow necrotic material is situated. The swollen Peyer's patches in the lower portion of the ileum show, scattered over their surface, numerous ulcerated areas, capped with this same yellowish necrotic material, varying in diameter from 4 mm. to considerably over a cm. The edges of all these ulcerated areas are, in places, distinctly hemorrhagic and, as a rule, the blood-vessels of the intestinal wall can be seen radiating from the edges of the lymphatic apparatus, filled with blood. The lymphatic apparatus of appendix is markedly swollen, but no ulcerations are present. The upper portion of the colon is thickly dotted with swollen solitary follicles. These have an average diameter of about 7 mm., are considerably raised above the surface of the intestine, and show on their inner surface ulcerated areas capped by yellowish necrotic material similar to those seen in the small intestine. They differ from these latter from the fact that their bases are, as a rule, distinctly hemorrhagic, each nodule being surrounded by a distinct zone of submucous hemorrhage. The lower part of the colon is almost entirely free from such areas, but contains a number of discrete or confluent pin-head areas of hemorrhages.

Mesenteric Glands.—Particularly those behind lower portion of ileum are extremely swollen. They are soft in consistency and on section have a mottled appearance, the predominating color being a bright pink, the mottling being due to pin-point gray areas, which are scattered through them, perhaps the swollen follicular portions of the glands.

Anatomical Diagnosis.—Typhoid fever (beginning of second week), with typhoid septicæmia. Swelling of Peyer's patches and the solitary follicles with superficial necrosis and ulceration. Marked involvement of the solitary follicles in the upper portion of the colon. Great swelling of the mesenteric glands. Acute spleen tumor. Cloudy swelling of the heart muscle, liver and kidneys.

The microscopic examination of the heart, lungs, and kidneys adds particularly nothing to the macroscopic observations, except that the heart muscle showed the evidences of a moderate degree of fragmentatio myocardii. The following are the notes from the protocol regarding the microscopic appearances of the liver, spleen, mesenteric glands, and intestines:

Liver.—Capsule is everywhere normal in appearance. The connective tissue is not increased in amount. Liver cells are greatly swollen and extremely granular. Scattered throughout the liver substance are numerous, almost circular areas, presenting varying appearances, according to the stage of development. In some instances the areas show merely an extensive necrosis of the liver cells, many of them in such areas having lost their nuclei, this loss of nuclei giving rise to a light colored patch in the liver substance. Many of the other areas show, besides this necrosis, an infiltration with cells of varying characters. In some of them the necrotic area is infiltrated, for the most part, with small round cells of the lymphoid type. In others, large numbers of irregularly shaped epithelioid cells are present. No giant cells can be made out. The nodules resemble very markedly, in some instances, miliary tubercles, but there is not present a definite arrangement of the two varieties of cell, such as exists in tubercle; but, on the other hand, the two forms are evenly intermingled in the nodules. These nodules apparently bear no definite relation to any particular anatomical structure of the liver in most instances, although at least in one instance the necrotic area lies exactly around the central vein of the lobule. Besides areas of necrosis, there are found scattered through the organ a number of blue-staining areas, usually of much less extent than those occupied by the nodules. These areas have a granular appearance under the low power and which is more marked under the high power. It can be seen, at the edges particularly, that they are made up of individual rod-like structures resembling the typhoid bacilli. The blood-vessels of the liver show no particular change; nor do the bile-vessels.

Spleen.—Capsule not thickened. Trabecular substance is normal in amount. The amount of blood present in the pulp is tremendously increased over the normal. Furthermore, it can be made out with the high power that in a great many instances the red-blood corpuscles are contained in large cells. Scattered throughout the organ are a number of almost circular areas, in which it can be seen with the high power that considerable necrosis exists, as is shown by lack of nuclei and many of the spleen cells, and by the presence of nuclear fragments. These areas, as in the liver, are often infiltrated with lymphoid and epithelioid cells. There are also present in the spleen numerous blue-staining granular collections of bacteria similar to those seen in the liver. In some instances these collections of bacteria are in definite relation with necrotic areas, but this could very rarely be made out in the liver.

Mesenteric glands.—The amount of normal gland structure is very small. Almost the entire gland appears to be in a necrosed condition. In some areas the necrotic foci contain very large quantities of fragmented and destroyed nuclei. In other places very few of these are present. Among the necrotic areas are to be found, as in the liver and spleen, numerous epithelioid and lymphoid cells, some of these latter doubtless being cells which normally belong to the lymphoid glands. The areas of necrosis may possibly have been focal in origin, but in the section under observation they are so extensive that one coalesces with the other all over the gland. There are apparently no clumps of bacteria in this section under observation.

Intestines.—The lesions of the intestine vary. In all cases the superficial layer of the intestine seems to be necrotic to a certain extent, but this at any rate is doubtless due partly to post-mortem change. In the earliest stage of the disease to be made out in these sections, the lymphoid apparatus is tremendously swollen, the cells present in the swollen area no longer being apparently lymphoid in character, but many epithelioid cells are also present. All through the swollen area there are evidences of necrosis in the form of numerous nuclear fragments. In the earlier stages the muscular coat of the intestine

does not appear to be affected. The section which shows a more advanced stage of the disease shows that the progression consists mostly in the extension of the necrotic processes. In some instances the whole involved area is entirely necrotic, almost to the depth of the muscular coat, and there may be present beneath this necrotic material and between it and the muscular coat fibrin, in whose meshes are entangled polynuclear leucocytes and epithelioid cells. In this stage the muscular coat itself usually shows the presence of a few polynuclears and a large number of small round cells or epithelioid cells. Elsewhere in the swollen areas the necrosis is extensive, as in the mesenteric lymph glands. There is hardly an area in the section which has escaped it. In the later specimens the amount of cellular infiltration in the muscular coat is often very large, the muscle fibre being pushed widely apart by it, and in some places being distinctly necrotic over large areas. The infiltrating cells, under these circumstances, seem to be mainly small, round and epithelioid cells with an occasional polynuclear. Blue-staining collections of bacteria are seen in very large numbers in the deeper part of the necrotic areas in some of the sections.

Bacteriologic Report.—Coverslips from the mesenteric glands, spleen and bone marrow all show the presence of medium-sized, short, thick bacilli frequently occurring in clumps. Cultures were taken upon slant agar-agar from the heart's blood, spleen, lung, liver, mesenteric glands, kidney, and bone marrow.

The culture from the heart's blood, after 24 hours' incubation, contained four discrete pinhead-sized, gray-white, slightly elevated colonies. The morphologic appearances showed the presence of a bacillus of moderate length and thickness, apparently a pure growth. Culturally the organism behaved as follows:

Litmus milk.—No acidification or coagulation of the milk after six days' incubation in the thermostat at 37½° C.

Potato.—A moist, just perceptible growth along the line of inoculation.

Bouillon.—Diffuse cloudiness of the nutrient medium. Hanging drop preparations from young cultures show active motility.

Gelatin stab.—Whitish growth along the line of inoculation; no liquefaction of the gelatin.

Dunham.—Diffuse cloudiness of the medium. No indol reaction. No gas formation in saccharose, glucose or lactose media.

Agar slant.—Moderate, moist, whitish elevated growth. This organism, with the serum of an undoubted case of typhoid fever, showed a very positive Widal reaction in dilutions, varying from 1 to 30 to 1 and 50.

Diagnosis.—Bacillus typhosus.

The cultures from the spleen, liver, mesenteric glands and bone marrow similarly contained a pure growth of a bacillus, morphologically and culturally, like the organism isolated from the heart's blood. The typhoid bacillus was also isolated from the kidney associated with the bacillus coli communis. From the lung the colon bacillus was isolated in association with the staphylococcus pyogenes albus.

Case II.—James R., aged 36, admitted into the Albany Hospital, August 8, 1898, suffering from severe headache and pains in the arms and legs. The family history showed nothing of importance, and until the present sickness patient had always been quite well. Four days before admission he was taken ill with violent headache, fever, pains in limbs, and a slight chill. The following morning he went to his work, but felt so much worse that he went home and retired to his bed. The day before entering the Hospital he suffered from a nosebleed, and had another on his way to the Hospital.

The physical examination shortly after admission was quite negative, but the temperature was 102.2° F. Later on in the disease the liver became slightly, and the spleen very much, augmented in size. The bowels remained constipated from the beginning of the disease, and at no time did the patient complain of abdominal tenderness at any point. There was some vomiting on several occasions, but at no time was the gastric derangement very severe. Toward the end delirium came on. The temperature throughout the disease varied between 99.8° F. and 103°, until the day before his death when the temperature reached 105.2° F. Death August 25th, 1898.

The autopsy notes are as follows:

Body 175 cm. long, moderately well built, considerably emaciated. Rigor mortis in both extremities. Pupils wide and equal; mucous membrane pale; post-mortem lividity of dependent parts. Abdomen tense and very distended, apparently with gas. Walls discolored; patches of greenish blue. Subcutaneous fat nearly absent. Muscles of thorax and abdomen pale and poorly developed.

Peritoneum.—Both layers smooth, glossy and free from injection. Omentum free from adhesions and contains a little fat; omental glands not enlarged. Intestines very distended with gas, particularly small intestines. Left lobe of liver visible below costal margin 5 cm. Stomach not apparent. Peritoneal cavity contains a small quantity of dark-colored, turbid fluid. Appendix measures 13.5 cm. in diameter, normal in appearance and free from adhesions; mesentery present throughout its entire length. Diaphragm fifth space on right side; sixth rib on left. Costal cartilages not ossified. Retro-sternal glands not enlarged. Both pleural cavities free from any excess of fluid.

Pericardium.—Both layers smooth; cavity contains no excess of fluid.

Heart.—Contains red and chicken-fat post-mortem clots, and is distended with fluid blood; normal in size. The endocardium of the right heart shows post-mortem discolorations. Tricuspid valve normal; also pulmonary and semilunar valves. The left heart shows areas of fatty atheroma in auricle; ventricle normal. Mitral leaflets very thick along their free edges. Aortic valves normal. Aorta just above valve shows areas of fatty atheroma. Coronary arteries patent; walls show large confluent patches of fatty atheroma. Heart muscle somewhat soft; on section, of a dark reddish-brown color (brown atrophy).

Left lung.—Bound down by old firm adhesions at the base and posteriorly. The pleura elsewhere is smooth. Lung crepitant; less so in normal than lower lobe. On section, the upper lobe is slightly congested; lower lobe markedly so and

contains quantity of blood-stained serum, which readily escapes. Bronchial mucous membrane congested and covered by a moderate amount of mucus. One portion of the upper lobe contains a pea-sized, firm calcareous mass embedded in the lung substance proper.

Right lung.—Bound down by old firm adhesions laterally and posteriorly. Lobes very much increased in consistency, but still crepitant. On section, the three lobes generally present a similar appearance, and contain a large quantity of blood-stained serum, especially the lower lobe, from which it runs off in abundance. The three lobes are markedly congested. Bronchi and blood-vessels similar to other side. In several places are a number of nodules very firm, sharp, and circumscribed, varying from a small shot to large pea in size. On section, these nodules are calcareous.

Spleen.—Free from adhesions. The organ is very large, measuring 16x6x10 cm. Capsule not wrinkled, and smooth. Consistency much decreased. Trabeculæ not increased. Spleen pulp very much augmented. Malpighian bodies also very greatly augmented in size.

Liver.—Bound to the diaphragm and to the abdominal wall by adhesions. The organ is very much enlarged, measuring 26x20x8 cm. The capsule smooth. Consistency softer than normal. On section the organ is pale and cloudy (cloudy swelling).

Gall-bladder. — Distended with greenish-colored bile. Mucous membrane smooth and normal looking.

Left kidney.—Fatty capsule scanty. Fibrous capsule strips off fairly easily, occasionally tearing bits of kidney substance. The organ is somewhat enlarged. The surface is smooth; veins somewhat prominent. On section the cortex is practically normal in amount; markings quite prominent; glomeruli very distinct and congested. Medulla normal. Pelvis normal.

Pancreas, adrenals and left ureter are normal.

Mesenteric glands not enlarged, or only very slightly so.

Aorta shows occasional patches of fatty atheroma.

Retro-peritoneal glands.—Enlarged, but not markedly so.

The right adrenal gland occupies its normal anatomical position in relation to the surrounding viscera, but below it the kidney is absent. In its place is a small, somewhat firm, mass of tissue 5 cm. long and 2 cm. in thickness, and which, on section, presents a very peculiar appearance, in no manner suggestive of renal tissue. The ureter of this side leads to this mass.

Bladder.—Contains a small quantity of light, turbid urine. The walls are not increased in thickness and the bladder is of normal size.

Intestines.—The small intestines show no injection of the mucous membrane nor are the solitary follicles swollen. In the small intestine Peyer's patches show no evidence of being swollen or of other implication. No evidence of ulceration or cicatrization. The mucous membrane of large intestine is quite normal in appearance.

Anatomical Diagnosis.—Marked œdema and congestion of both lungs; chronic adhesive pleuritis and healed (calcareous) tuberculosis of both lungs. Brown atrophy of heart. Acute spleen tumor; cloudy swelling of liver and kidney; congenital absence of right kidney; slight swelling of mesenteric glands; fatty atheroma of aorta; coronary artery disease.

The microscopic examination of the heart shows some fragmentatio myocardii in addition to the macroscopic findings; the lungs and kidneys microscopically show nothing very striking.

The following are some notes abstracted from the records of the microscopic examinations of the liver, spleen, and mesenteric glands:

Liver.—Capsule is normal in thickness. Connective tissue of the organ does not appear to be increased. The liver cells are swollen and rather indistinct. The nuclei are apparently, as a rule, well preserved. Scattered throughout the section in large numbers are circumscribed areas of focal change. In places as many as three of these can be seen under a low power. The appearance exhibited by these areas varies in different parts of the section. In some of them the process seems to be almost entirely necrotic in character, the liver cells in the area having lost their nuclei and taking rather an intense stain with the eosin. In these areas can be seen a few polynuclears and a number of small, round cells and cells of an epithelioid type. In other portions of the section the areas are extremely cellular and have the typical appearance of lymphoid nodules. In these instances the cells in such an area are either small or round cells, or rather long, irregular cells of an epithelioid type. There are no giant cells present, and the appearance of these nodules does not suggest tubercles. The nodules have apparently no connection with the vascular system of the organ. Besides these nodules, there can be seen occasionally in the liver substance patches of rather diffuse blue-staining material, which, under the high power, are seen to be composed of small rods, presumably bacteria. The hepatic vessels and the bile ducts are apparently normal. In one field one of the bacterial patches described above is present in one of the areas of necrosis, but as a rule no such association exists.

Spleen.—The capsule is not increased in thickness. Trabeculæ appear normal in amount. The Malpighian bodies are rather large, but otherwise show no change. The pulp contains an excess of red-blood corpuscles, which are scattered irregularly among the pulp cells. Some of these can be seen to be inside of large phagocytic cells. In a few places in the substance of the pulp there are sharply localized areas in which the spleen substance has become necrotic. There are present in these areas a moderate number of cells; a few of which are polynuclears, the rest either small, round cells or cells of an epithelioid type. The blood-vessels of the organ present about a normal appearance.

Mesenteric glands.—Show extensive changes in the form of localized or diffuse areas of necrosis. These seem to be most marked in the central portions of the glands, but they are also present in the periphery. The necrotic areas stain rather sharply with the eosin, and contain large numbers of nuclear fragments, some polynuclear leucocytes, and a fair number of round cells and cells of an epithelioid type. In one or two places in the sections there are to be seen diffuse areas of blue-staining which, under the high power, are seen to be made up

of masses of bacteria. These have no connection in any of the sections examined with the areas of necrosis.

Sections of the liver, spleen, kidney and mesenteric glands, stained by Flexner's methylene-blue method, showed masses of bacilli, resembling, morphologically, the typhoid bacillus.

Bacteriologic Examination.—Cultures were taken at the time of the autopsy from the heart's blood, lung, liver, gall-bladder, spleen, kidney and urine. From all of these, with the exception of the kidney and urine, one single organism was isolated which, morphologically, was a somewhat short, moderately thick bacillus which decolorized by Gram's method of staining. It grew upon media as follows:

Agar slant.—Abundant, moist, white, elevated growth.

Blood serum.—A growth very similar in appearance to that on agar.

Potato.—A moist, slight, almost invisible growth.

Bouillon.—A diffuse cloudiness. Hanging-drop preparations show a well-marked motility of the bacillus.

Dunham.—A diffuse cloudiness; no indol reaction could be obtained.

Litmus milk.—After several days it acidified milk, but failed to produce any coagulation.

Gelatin stab.—Moderate white growth along line of inoculation, but no liquefaction of the gelatin.

No gas formation in saccharose, lactose or glucose media.

Cover-glass preparations, stained by Pittfield's method, showed the flagella with a peritrical arrangement. Tested with known typhoid serum, the bacillus produced a typical Widal reaction in 12 minutes with a dilution of 1 to 10; in 42 minutes with a dilution of 1 to 100.

Diagnosis.—Bacillus typhosus.

The cultures from the kidney and urine contained the typhoid bacillus, but associated with an organism giving all the tests for the bacillus coli communis.

The possibility of the existence of typhoid fever without intestinal lesions was long since conceived by Louis[40], who, himself in Observation 52 of his book, reported an instance that during life presented a typical clinical picture of typhoid fever. The patient died on the 55th day of his disease, and the necropsy showed absolutely no existence or evidence of recent implication of the intestinal canal. The belief of the occasional existence of typhoid fever without anatomic intestinal changes was entertained by a number of the earlier clinicians after Louis, but the clinical simulation of enteric fever by other maladies necessarily, in the absence of bacteriologic criteria, makes these reported cases less valuable as contributions to the study of this rare type of typhoid fever. The conclusive demonstration of this form, without intestinal lesions, dates since the discovery of the specific organism of etiologic importance, and more especially from the time when the differentiation of the typhoid bacillus from allied species became more firmly established. In addition to the reported cases of Banti[41], Karlinski,[42] Guarnieri[43], Vaillard[44], Chantemesse[45], and Vincent[46], other instances carrying more conviction have been published by more recent writers.

DuCazal[47], in 1893, reported the case of a young man, 21 years of age, who had been ill for fifteen days before entering the Hospital. The clinical history suggested typhoid fever, subsequently complicated by double pneumonia. At the autopsy the principal lesions were pneumonia of both lungs and acute spleen tumor. The intestines showed absolutely no evidence whatever of any anatomic alterations, but the cultures from the spleen contained bacilli, morphologically similar to, and on media behaving like, Eberth's bacillus. Kühnau[48] some years later published an interesting observation of this kind. The patient was a pregnant woman, 32 years old, who developed typhoid fever with the subsequent development of erysipelas of the face. Bacteriologic examination of the blood during life showed typhoid bacilli, as already mentioned. The woman died, and the post-mortem examination showed enlargement and necrosis of mesenteric glands, abscesses of the kidneys and thrombosis of one of the ovarian veins. The intestines were free from any lesions whatever. The bacillus typhosus was cultivated from the kidneys, mesenteric glands and spleen.

The case of Pick[49] was that of a 23-year-old woman, who died in the fourth week of a typhoid fever. During life the Widal reaction was positive. The anatomic diagnosis of the autopsy was: Typhoid infiltration of the mesenteric lymph glands, parenchymatous degeneration of organs, and left-sided lobular pneumonia. The spleen was not enlarged and the intestines were free from lesions. The serum test after death was positive in 1 to 10; cultures from the gall-bladder and mesenteric glands contained the typhoid organism; that from the spleen was negative.

Meunier[50], at the séance of the Société Méd. des Hôp. de Paris of April 7th, 1897, reported an uncommon observation of typhoid infection in a boy, 8 years of age, suffering from acute miliary tuberculosis. Shortly after admission into the Hospital rose-spots appeared and the application of the Widal test gave a positive reaction. The lesions found at the necropsy were tubercular ulcers of the intestine. Typhoid bacilli were demonstrated in the cultures from the spleen, lungs and pleural exudate.

Beatty[51], about the same time, published a case of typhoid fever, commencing with nausea and pain in the back followed by jaundice. Death on the sixth day. The examination after death showed an enlarged spleen and mesenteric glands, but in the intestines there was an absence of lesions. The spleen contained typhoid bacilli.

Chiari and Kraus[52], in a very recent and valuable article, have discussed the subject very exhaustively and reported seven cases of atypical typhoid infection, in which there was an absence of anatomic lesions of the intestines. These observers classify enteric fever into four great anatomic divisions: The first include all those cases presenting the characteristic typhoid lesions; the second those anatomically atypical but, nevertheless, recognizable cases on the autopsy table; the third comprising that class of cases characterized by an absence of anatomical lesions, making the diagnosis, anatomically, impossible, but in the organs of which typhoid bacilli are found; and finally, the last group to include such cases as cannot be diagnosticated anatomically or bacteriologically, but which give positive serum reaction with the Widal test. Group III, of this classification, is of particular interest to us, inasmuch as the Case II, reported in our paper, belongs to this class. The

typhoid septicæmias frequently fall under this heading. Of the five cases reported by Chiari and Kraus as belonging to this group, only three were based on the presence of the typhoid bacilli in one or more of the organs. The diagnosis of Cases XV and XVI is entirely based on a positive result of the serum test, no typhoid bacilli having been demonstrated in any organ. Although, with proper precautions and in sufficiently high dilutions, the specificity of the serum reaction is almost absolute, nevertheless certain errors must necessarily arise at times, and these become increasingly great as the dilution is made lower and lower. Chiari and Kraus used dilutions of 1 to 10 and 1 to 12, degrees of dilution particularly susceptible to fallacious results. In view of this, Cases XV and XVI lose much of their interest as examples of typhoid fever without intestinal lesions. These remarks likewise, in our opinion, apply with equal force to Case XVIII and all the cases of group IV, the diagnosis of all of which being based on the serum reaction with very low dilutions.

Flexner and Norman Harris (53) very recently have contributed a very carefully studied additional example of typhoid infection without intestinal lesions. The case was that of a man, 68 years of age, who suffered from shortness of breath, symptoms of pleuritis, and finally died two days after admission into the Hospital. The autopsy, performed one hour after death, showed thrombosis of pulmonary artery, gangrene of lung, perforation of pleura, pyo-pneumo-thorax, acute spleen tumor, parenchymatous degeneration of liver and kidneys. The mesenteric glands were not swollen, and the intestines showed nothing abnormal. The bacteriologic examination demonstrated the presence of typhoid bacilli in liver, spleen and lung.

Examples of typhoid fever, without intestinal implication, are not entirely limited to adults, but, on the contrary, the apparent small disposition to intestinal lesions of very young children suffering from this disease is one of considerable interest in this connection. Chantemesse and Widal (54) called attention to the trivial character of the intestinal lesions in the young some years ago; and Brouardel and Thoinot (55) likewise mention this peculiarity, as does also Marfan (56). The publications of Etienne (57), Freund and Levy (58), and others, include cases of this character in which the intestinal lesions were at a minimum or totally absent.

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CAVITIES IN THE BRAIN PRODUCED BY THE BACILLUS AEROGENES CAPSULATUS.

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AND

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Reports of cases of subcutaneous and visceral invasion by gas-forming bacilli are multiplying rapidly. Chas. Norris[1] has given the most recent monograph on general infection by the bacillus aerogenes capsulatus. He reviews most of the recent literature and enters especially into bacteriological experimentation. The following case is of interest because the bacilli seemed to have had a predilection for the brain.

HISTORY OF CASE.

Mrs. C. B. Age, 35. Colored. Admitted to the Surgical Ward of the Maryland General Hospital, suffering from shock caused by a gunshot wound of the abdomen. Prof. J. D. Blake was summoned and performed a laparotomy, suturing several perforations of the intestine. The bullet was not found. After applying the dressings the patient was put to bed and rallied from the operation very well. There was a slight rise of temperature the first day, but this soon subsided and it seemed as though an uneventful recovery would ensue. There was no pain or distention of the abdomen. Temperature and pulse normal, bowels constipated. On the third day a change in her condition was noticed. She seemed to be getting weaker without any appreciable cause. In a few hours after the change was noticed she quietly passed away. At the autopsy, which was performed 24 hours after death, the following condition was found: Body that of a strongly built and well-nourished negro woman. Rigor mortis marked. No crepitation of subcutaneous tissue. On opening the abdominal cavity the viscera appeared normal. The perforations were healing nicely; no indications of peritonitis. The bullet was found in left iliac muscle. On section of the various organs there were no appreciable signs of gas formation except in the uterus. Here a number of small spaces were seen. No gas could be detected, and on microscopical examination no bacilli were found. The heart and lungs were normal. The dura mater was found closely adherent to the calvarium. The brain was removed, surrounded by its meninges, and placed in a 4 per cent. solution of formalin to harden, before sectioning. The spinal cord was not removed. The external aspect of the brain was normal, the sulci and gyri being especially well marked. After the brain was thoroughly hardened (4 to 6 days), horizontal sections were made from the base upward, which revealed the following condition:

In the right hemisphere there existed a large cavity, involving the external capsule in its entirety, being five centimeters long, one centimeter broad and two centimeters deep, which appeared to be lined by a smooth glistening membrane. A small amount of bloody serum was found in it. Throughout the lenticular nucleus numerous small cavities were found, varying from one-half to one centimeter in extent. The anterior limb of the internal capsule, on a level with the middle commissure, contained several cavities, also a small one in the optic thalamus. Another section made on a level with the velum interpositum showed the posterior limb of the internal capsule to be almost completely destroyed by two large cavities. None of these spaces communicated with the ventricles. The caudate nucleus was intact. In the external orbital convolution a large cavity existed, being three centimeters deep and one centimeter broad, apparently lined by a smooth membrane.

Left hemisphere was smaller than the right. The first section revealed a cavity in the anterior limb of the external capsule two centimeters long and one centimeter deep. In the posterior limb 3 to 6 small pits or depressions were seen. In the lenticular nucleus several large excavations. The fibres of the internal capsule on this side seemed to pass around the cavities. The caudate nucleus and optic thalamus were normal. The cavities on this side were not as large nor as extensive as on the opposite side. The sulci and gyri were especially well marked, the former being very deep. No cortical or subcortical lesions were found. On section the cerebellum showed a few small subcortical cavities in the arbor vitae, superior surface. Otherwise, it was normal. After seeing this honeycombed appearance of the basal ganglia, the question immediately arose as to the cause. Was it congenital or acquired? Could the woman have lived in this condition without manifesting any symptoms of cerebral trouble? Could it be porencephalia? Was it produced by formaldehyde? These and numerous other surmises were not answered until sections were made and examined microscopically.

We submitted several sections to Dr. Barker, who at once recognized the bacteria as the cause of the cavity formation.

On studying sections under the low power of the microscope, the edges of the cavities appear quite smooth, and the clean-cut appearance seen in the gross sections of this brain again shows itself. They are devoid of any membranous or epithelial lining. Indeed, some of these cavities are surrounded by comparatively normal tissue, the brain cells in some instances forming the very edge. This is, however, an exception; for surrounding most of them is an area of cell degeneration of variable thickness, which is easily recognized by the absence of nuclear staining; indeed, the absence of all cellular structure is frequently seen in this zone, so that a diffuse homogeneous staining with eosin divides this from the zone to be described next. On passing outwards, this advanced stage of degeneration is gradually superseded by one in which only a partial loss of nuclear staining is evident and staining of the individual cells appears. Lastly, this zone merges into normal brain tissue. As for the spaces themselves, they are usually quite empty, excepting for certain masses which take on a deep hæmatoxylin staining and under the low-power lens have a somewhat granular appearance; not infrequently these masses lie imbedded in the

walls of the cavities; but what is especially striking, is that by far the majority of the capillaries in the section are completely filled by them. When examined under a higher lens (No. 7 or oil immersion), it becomes evident that these darkly staining masses, just mentioned, represent aggregations of bacilli, and, as far as we can judge from microscopical appearances alone, they are pure growths of a bacillus having the following morphology:

A fairly long, rather thick, bacillus, varying at times in either dimension, at times in both, with an average length from 3 to 6 mm., and with the comparative thickness of the anthrax bacillus; its ends are slightly rounded; the organism occurs singly, in pairs and clumps, and in parts of these specimens as chains. It stains with the ordinary aniline dyes; also by Gram's method. No spores were found, but no special stain was used for their demonstration. The bacilli frequently lie free in the tissues at some distance from cavities, and their clumps are almost invariably surrounded by zones of cellular degeneration, such as have been described surrounding the cavities; similar cellular changes are frequently seen in the neighborhood of bacilli which lie within blood-vessels. Judging from these specimens it would seem that the veins and capillaries are especially active in carrying the organism, for those arteries with well-marked walls showed as a rule, with one or two exceptions, no bacilli in their lumina. As to the part played by the lymphatics in such a conveyance it is difficult to say; we believe they played a minor rôle in this case. In none of the perivascular lymph spaces (space of His) could we find the organism.

In no portion of the specimen were there any changes pointing to an inflammatory reaction, the entire absence of small-cell infiltration being very striking.

There are no hemorrhages in the brain tissue, nor could we detect the presence of blood in the cavities.

The arteries throughout are normal, showing no evidence of sclerosis. Any attempt at repair was entirely wanting, there being no neuroglial hyperplasia nor formation of granulation tissue.

CONCLUSION.

We believe that the cell degenerations and cavity formation in this case are due to the presence of the bacilli described, and that they belong to the class of gas-forming bacteria, the gas formation being directly responsible for the presence of the cavities, and the cellular changes being due to the action of toxins.

In 1892 Welch and Nuttall[3] reported in the July-August number of the Johns Hopkins Bulletin their discovery of a gas-forming bacillus obtained from the emphysematous tissues and blood of a man dead of aneurism of the aorta, for which they proposed the name, bacillus aerogenes capsulatus. Gas bubbles were abundantly present in the internal organs, notably in the myocardium, the liver, spleen and kidneys. This gas burned with a pale-bluish, almost colorless flame, a slight detonation being heard at the moment of ignition.

Upon microscopical examination of these organs, they found around masses of bacilli frequently, but not always, a disappearance of the nuclei and degenerative changes in cardiac muscle cell, and the epithelial cells of the liver and kidney, especially in the neighborhood of gas cavities, in the walls of which the bacilli were often densely accumulated.

They describe the bacillus aerogenes capsulatus as follows:

The bacillus is non-motile, straight or sometimes slightly curved, variable in size, but averaging about the thickness of the anthrax bacillus, and from 3 to 6 cm. in length, with adjacent ends slightly rounded or sometimes square cut; occurs singly, in pairs, in clumps, and sometimes in chains, and stains readily with the ordinary aniline dyes, and after using Gram's method, staining is either uniform or with small unstained spots, less frequently with isolated deeply staining granules.

Capsules, although not constant, were frequently demonstrated, especially by Welch's method for staining capsules in specimens from the animal body and sometimes from agar cultures. No spores were found either in the animal body or in cultures.*

The bacillus grows upon all ordinary culture media under anaerobic conditions, at body temperature slowly; at 18 to 20 C. no growth on surface of solid media under ordinary conditions. Gas is produced in all cultures containing fermentable material. Time and space will not permit us to describe the cultural characters more in detail, and those interested in this subject are referred to the original paper and also to that of Welch and Flexner in the Journal of Experimental Medicine, Vol. I. This organism is non-pathogenic to rabbits even when a pure culture is injected into the circulation.

If the animal is, however, killed immediately or soon after intravenous injection, after 4 to 6 hours at 30 C., or about 18 hours at 18 or 20 C., there follows great gas formation in the blood-vessels and organs and the bacilli are found abundantly in these tissues.

Although we cannot prove in the absence of cultural growths of the organism found in this brain that the bacillus under consideration is identical with that described by Welch and Nuttall, there seems to be little doubt from the resemblance in morphology, staining characteristics and more especially in its reaction to Gram's method, and last but not least, in the changes which it produces in the tissues, that this organism is at least closely allied to the bacillus aerogenes capsulatus and probably identical. As animal experiments show this organism to be non-pathogenic, and clinical experience, with a single exception, tends to show that general infection with this organism takes place immediately before or after death, practically the latter only, as far as can be judged from the symptoms due to general gas formation in the body; and further, as there is no evidence in this case which points to a general infection by this organism, before the death of the individual, we concluded that the changes occurred post mortem, the distribution of the organism most likely occurring in the preagonal period. The organism not infrequently produces localized emphysematous conditions only in the tissues, from which recovery usually takes place because it seems essential for the existence and growth of this organism

* Since this publication Dunham has found that this organism produces spores when grown on blood serum.

that the tissues must have been previously injured or that the blood-supply should be poor in oxygen. That an injury may be trivial and still favor its development seems quite clear from two cases reported by Fraenkel,[3] in which infection followed hypodermic injections, in one case after the injection of camphor, oil and ether under the skin, and in the other of a dilute solution in water of sulphuric acid and chloride of morphia. One of these cases pursued a rapidly fatal course, death occurring two days after the injection. Before the discovery of this organism the cause of death in such cases would very likely have been attributed to the entrance of air into a vein. Welch and Nuttall in their original paper expressed the belief that many of the deaths attributed to the entrance of air into the veins would prove to be cases of gas bacillus infection, and especially referred to cases occurring in obstetrical practice in which it was supposed that air had entered the uterine cavity and had been absorbed by the uterine sinuses thus causing fatal air emboli. Perkins[4] reports such a case following an attempt at criminal abortion, and attributed the fatal outcome to air embolism. Dr. Dobbin,[5] of the Johns Hopkins Hospital, through the kindness of Dr. Perkins, had an opportunity of studying sections from the uterus in this case and found the characteristic lesions of gas bacilli infection, the bacilli corresponding in morphology and staining characters to the bacillus of Welch and Nuttall.

The "Schaumorgane" of the Germans are due to such infections and the elaborate article of Ernst[6] on the "Schaumleber" is especially rich in the microscopical changes in the tissues. He describes the microscopical appearance of the "Schaumleber" as follows: "On making the usual single long transverse section through the liver, the two portions thus formed fell apart almost immediately, and while examining these gas bubbles I saw that they began to appear from the larger vessels soon in such numbers that hillocks of froth were formed on the surface of the section; these hillocks gradually coalesced. If these masses of froth were stripped away, hardly a few minutes passed before fresh ones had formed. This condition of re-formation of froth continued for a long time. The autopsy had been performed 3 hours after death and there were no evidences of decomposition."

In reviewing the literature on this subject one clearly sees that these infections with gas-forming bacteria are becoming more widely recognized, and the number of articles have increased every year since the appearance of those of Welch and Nuttall and that of Ernst. In fact, at present the changes due to these bacteria have been described in almost every organ, including, for instance, the liver, spleen, stomach, intestines, bladder, kidney, uterus, skeletal muscles, etc. Notwithstanding this, we have been unable to find any description of pathological changes attributed to these bacteria in the brain or spinal cord, which seems indeed strange if one considers the comparative frequency of these infections and that they are fairly well recognized by observers in general. One can hardly believe that the central nervous system should be spared from such changes in cases of general infection where almost all organs may show the presence of gas cavities. Of course that the liver, spleen, and perhaps the uterus may predominate in showing the presence of these cavities when once the general circulation conveys the organism is not difficult to understand, for as the veins seem to be especially employed in such a conveyance it is no more than natural that organs which are abundantly supplied with large veins and therefore containing a large amount of the blood after death would contain a relatively greater number of the organism than an organ in whose parenchyma the veins were less abundant and the venous radicles of small calibre. The brain and cord can certainly be classed with those organs possessing a comparatively small amount of blood in their parenchyma after death; of course the membranes covering them must be excluded, for in these the veins being large, and containing a large amount of blood, in all probability an examination would, in the great majority of instances of general infection, reveal the presence of the organism. Of course the smaller venous radicles of the brain parenchyma would also contain a fair number of the organism, but these might be present in insufficient numbers to produce sufficient gases to give rise to appreciable microscopical lesions. We refer here, of course, more especially to cavity formation. The above is only a theory intended to cover the inference that probably in a great number of cases of gas bacillus infection showing gas cavities throughout the organs, the brain and spinal cord will in the great majority be spared. But in looking over the articles on this subject one can easily see why such changes in the central nervous system should have been overlooked and that in the report of cases coming to autopsy we have been unable to find, with one or two exceptions, any mention of a removal of the brain or cord, and it is more than likely that this was neglected, for had they been examined mention of this fact would undoubtedly have been made—this of course is a very evident reason for the non-recognition of similar changes as are described in this brain. Although this is, as far as we know, the first case in which cavity formation has been attributed in the brain to the presence of gas bacilli we do not claim that such changes have not been described before, but they have been explained by different etiological factors. Of such an instance we have found but two clear examples; both the brains are described by the same observers, namely, by G. H. Savage and W. Hale White, in an article entitled "Causes of Holes in the Brain," appearing in the Transactions of the London Pathological Society, Vol. XXXIV, 1882. These brains the authors obtained from two general paralytics, and as the kidneys, liver, lungs, and heart muscles contained cysts, they very naturally describe the changes by the term of "Universal cystic degeneration." In reading this article one is struck with the admirably clear description of the pathological changes. The illustration of the brain presented herewith shows a picture almost identical with the one reported by us, so that we feel little hesitancy in ascribing the changes described by Savage and White to the bacillus aerogenes capsulatus or an allied organism. A short résumé of the description of the brains and the changes in the other organs will not be out of place.

"Taking first the kidney, sections appear to show that in our cases .... the cystic change is due to dilatation of either the Malpighian capsules or cortical tubules. And in the liver .... the cysts appear to be due to small vacuoles in the

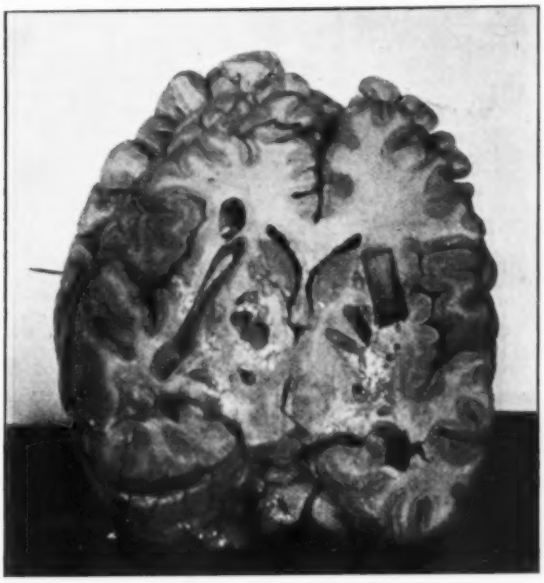

FIG. 1.—Photograph showing cavities in the corpus striatum.

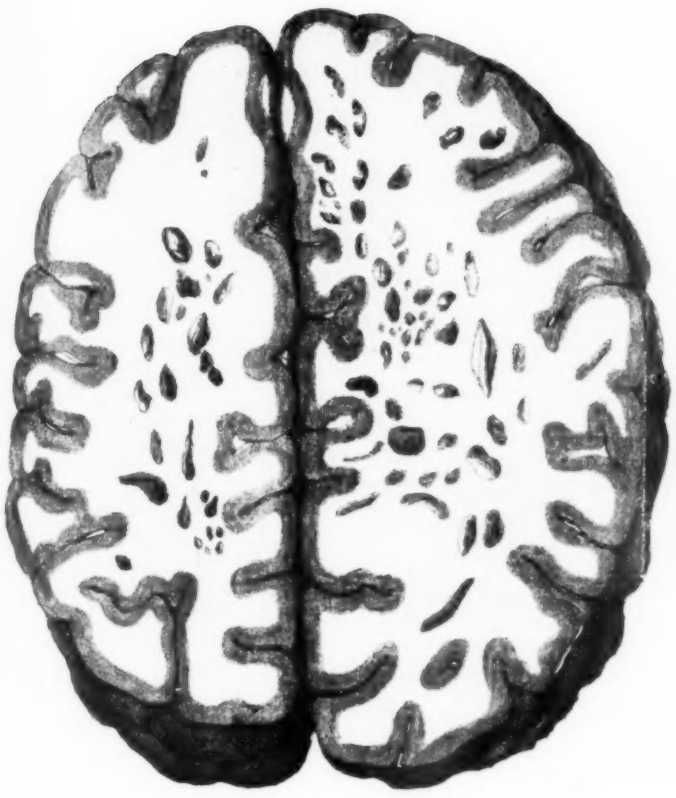

FIG. 2.—Reproduction of section of brain from Hale White and Savage's case of "General Cystic Degeneration." [Transactions of Pathological Society of London, Vol. XXXIV.]

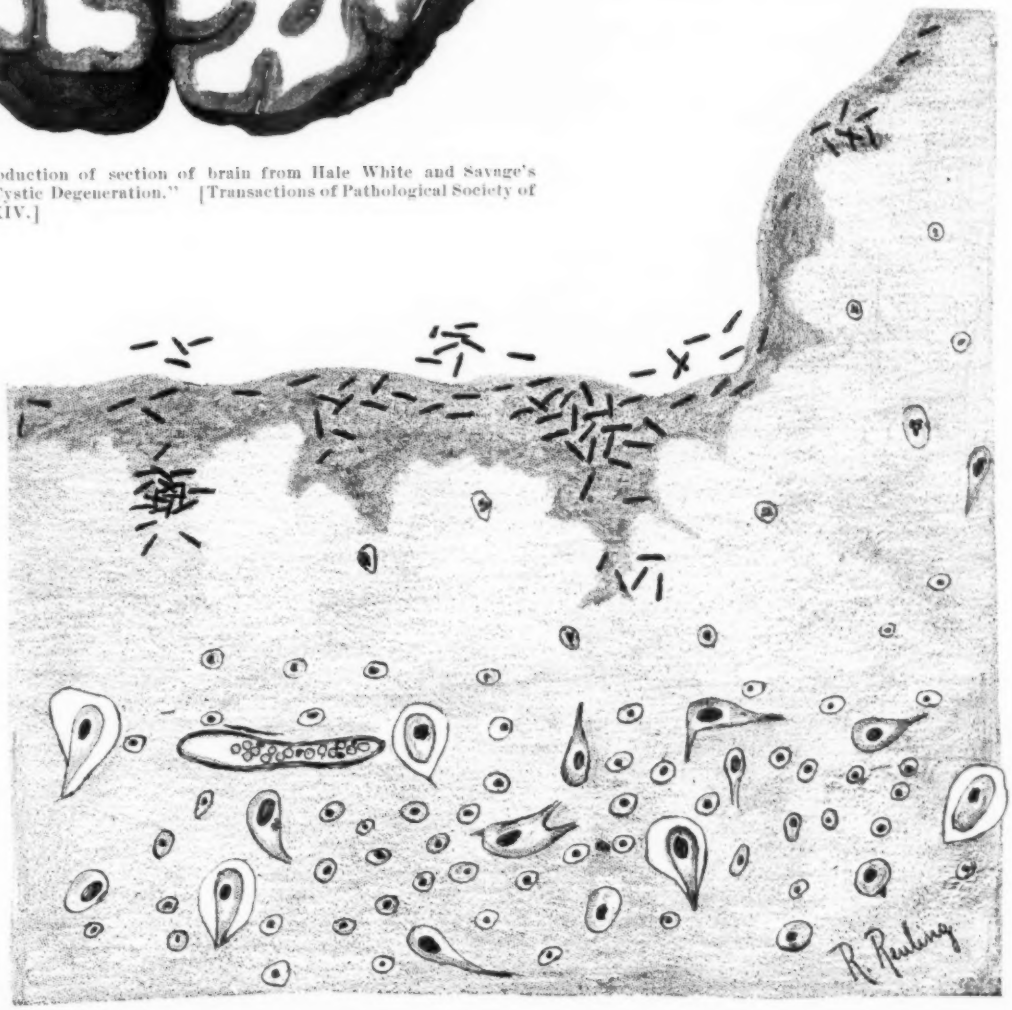

FIG. 3.—Section showing edge of large gas cavity with bacilli in its walls. Surrounding this is an area of cellular degeneration. (Immersion lens.)

hepatic cells, which we have proved not to be fatty by their refusal to stain with osmic acid. The several vacuoles in the same cell, by increase in size, run together to form one that occupies nearly all the cell, which being so distended bursts. The vacuoles of adjacent cells thus coming together soon form one large cyst. . . . . By this process in parts of the liver the cysts produced are so numerous that the whole organ has the appearance of a sponge; this is very well shown on holding up one of the microscopic slides. . . . . We do not think the hepatic cysts have any true wall, but the appearance of one is often produced by the cyst in the course of its enlargement coming in contact with some fibrous tissue, which it stretches and pushes before it, so that at last it appears to have a thin lining membrane."

"*Lungs*—The cavities are mostly circular and not connected with bronchial tubes; they contain no lining membrane. They have a tendency to occur in groups, and seem to be situated indiscriminately among the air-cells, from which they are distinguished by their regular shape and containing no granular epithelial debris, but in many cases the cysts have in the interior a peculiar amorphous matter which takes the logwood stain with great brilliancy."

Before going any further we wish to call especial attention to the mention of this "amorphous matter" which takes on the logwood stain so deeply, which the authors describe in the cavity of the brain and in the vessels of the different organs; this seems especially important as this "amorphous matter" which they describe is undoubtedly composed of masses of bacteria which the reader will remember often completely filled the vessels in the brain we describe and were so abundant in the walls of the cavities. Savage and White give only a short description of the appearances of the brain, but substitute for this a good illustration of the specimen. The description of the microscopical appearances of the brain cysts corresponds in all particulars to those found in the other organs. It would be useless for us to go into a minute comparison of the changes described in the case reported in this article and the other pathological conditions giving rise to cavity formation in the brain. One could hardly, after a careful consideration of such conditions as porencephalia which has been so admirably treated by Kundrat' to which the reader is referred—the condition known as *état criblé*—is now considered by most observers as of no pathological significance and the holes in this are extremely small, generally of pin-point size and are frequently due to slight dilations of the Virchow-Robin lymph space, or by a shrinkage of the brain substance from the action of hardening fluids, causing a rather wide separation between vessels and parenchyma.

The holes produced in sclerotic processes found at times in the brain of general paralytics, and patients suffering from multiple sclerosis, could hardly take a form to resemble those cavities produced by this organism, as the former would almost necessarily contain a lining membrane, and evidences of neuroglial hyperplasia in different localities would speak for the chronicity of the process.

Discussion.

Dr. Welch—In connection with Drs. Herring and Reuling's contribution, it may be of interest to exhibit a microscopical section from a pig's liver which I examined to-day. I received the section from an eminent pathologist who was puzzled by the appearances. Two or three of the superficial lobules of the liver presented to the naked eye small, bleb-like spaces. The sections show a honeycombed appearance of the affected lobules, caused by an abundant development of bacilli identical, morphologically, with the B. aerogenes capsulatus. The gaseous spaces are sharply defined, and the appearances are indeed such as to be very puzzling, unless one is familiar with the blebs produced by the post-mortem development of our gas bacillus. The specimen is an example of emphysematous liver (Schaumleber), but is remarkable on account of the limited production of gas and the circumscribed arrangement of the holes, due in part to the large amount of connective tissue normally surrounding the hepatic lobules of the pig.

In the light of Drs. Herring and Reuling's observation, it is probable that certain cases reported in the literature as holes in the brain are really due to the post-mortem development of the gas bacillus.

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ACUTE FIBRINO-PURULENT CEREBRO-SPINAL MENINGITIS, EPENDYMITIS, ABSCESSES OF THE CEREBRUM, GAS-CYSTS OF THE CEREBRUM, CEREBRO-SPINAL EXUDATION, AND OF THE LIVER, DUE TO THE BACILLUS AEROGENES CAPSULATUS.

By W. T. Howard, Jr., M. D., *Professor of Pathology in the Western Reserve University, Pathologist to Lakeside Hospital, Cleveland, Ohio.*

(*From the Pathological Laboratory of Lakeside Hospital.*)

For the clinical history of the following case my thanks are due to Dr. Dudley P. Allen. H. E., male, white, aged 31 years, was admitted to Lakeside Hospital, service of Dr. Allen, March 22, 1898. His family history was without interest. The patient had had chicken-pox and scarlet fever, but denied syphilis.

In August, 1897, he contracted gonorrhœa, and shortly after this he noticed a painful swelling in the perineum. Six months later this ruptured, with the discharge of a considerable amount of pus. After this there was a permanent urinary fistula at this point. Three months after the occurrence of the first swelling another formed in the same region, and after the escape of pus healed and disappeared.

With the usual precautions under ether anæsthesia Dr. Allen curetted the fistulous tract which communicated with the urethra. After dilatation of the urethra a catheter was inserted and the wound allowed to heal.

A few days after the operation the patient became unconscious, developed symptoms of meningitis and died during the night of March the 29th, 1898. After the operation the temperature ranged between 99° and 104°, reaching 105° F. before death.

A few minutes after death the body was placed in a cold-storage chest kept constantly at 32° F.

The autopsy was begun ten hours after death.

Anatomical Diagnosis.—Operation for cure of perineal fistula. Acute fibrino-purulent cerebro-spinal meningitis and ependymitis, with abscesses of the cerebrum, gas-cysts in the cerebrum, cerebro-spinal exudation and in the liver, septicæmia (?), due to the bacillus aerogenes capsulatus; fatty degeneration of the liver, heart and kidneys; cloudy swelling of the kidneys.

The body was 182 cm. long, the surface cold, rigor mortis was marked. There was no œdema and no emphysematous crackling of the subcutaneous tissues. The abdominal muscles were well developed. The peritoneum was smooth and glistening. The pelvic cavity contained a small amount of slightly blood-tinged fluid with a few gas bubbles. The abdomen was not distended.

The chest was well shaped. The pleural cavities and the pleuræ were normal.

Both lungs were enormously congested and showed small areas of consolidation. On section a large amount of dark fluid-blood containing gas bubbles escaped. Gas bubbles escaped from the pulmonary vessels on pressure. The mucous membrane of the bronchi was deeply congested. The lungs were moderately pigmented. The bronchial glands were pigmented, but were free from tuberculosis. The mucous membrane of the trachea and larynx was congested.

The pericardium was negative. The heart was of ordinary size. The myocardium was pale. In the right auricle and auricular appendage and the right ventricle there were dark fluid-blood and loose clots, with a large number of large and small gas bubbles. The valves and coronary vessels were normal.

The liver was of ordinary size and its capsule smooth. On section a large amount of dark red blood containing large and small gas bubbles escaped from the hepatic and portal veins. The lobules were well marked; the consistencies were not specially increased. Scattered throughout the organ there were a large number of small opaque areas the size of a pin's head. The bile-ducts and the gall-bladder were negative.

The spleen was four times the ordinary size. The capsule was not thickened. On section the organ was soft, dark red in color and markedly hyperæmic. The Malpighian bodies and the trabeculæ were obscure. A large number of gas bubbles escaped on section.

The kidneys were of ordinary size. The capsules were readily removed. The surfaces were pale. The cortices were somewhat thicker than ordinary, and the glomeruli and veins were markedly congested. There were no gas bubbles to be found in the kidneys. The adrenals were negative.

The pancreas, œsophagus, stomach and small intestines were markedly congested. The colon and rectum showed nothing of interest. The testicles were negative. The urethra was normal; there was no stricture to be found. The perineal wound was healed, and no pus and no gas bubbles could be found. The right lobe of the prostate was larger than ordinary. No abscesses were found. The bladder was distended with urine. The mucous membrane was moderately congested; there were no ulcers. The pelvis was deep and narrow. Careful dissection failed to show any focus of suppuration. The pelvic veins, the inferior vena cava and the portal vein all contained large and small gas bubbles.

Head.—The scalp was of ordinary thickness and moderately congested. The skull was normal. The vessels of the dura-mater were moderately congested. The sinuses contained dark fluid-blood with large and small gas bubbles.

Brain.—The vessels of the surface of the brain were very much congested. The pia-arachnoid over the cerebral hemispheres showed a number of small opaque areas of fibrinous exudation. The structures at the base of the brain, including the nerves, were bathed in a thick yellow pus. The pia-arachnoid over the inferior surface of the cerebrum, a large portion of the cerebellum, the pons and the medulla were covered with a thick fibrino-purulent exudation.

On section of the left cerebral hemisphere just above the

Sylvian fissure, involving the intra-parietal fissure, and the ascending parietal and the supra-marginal convolutions, there was an abscess with soft, necrotic walls. This abscess varied from 0.5 to 2 cm. in diameter. Near this abscess at one side there were a number of smooth-walled cavities measuring from 1 to 5 mm. in diameter.

On the inner side, this abscess extended deep into the tissue. Occupying the anterior half of the left superior tempero-sphenoidal convolution there was an irregular abscess with soft necrotic walls. The abscess cavity was filled with a semi-fluid necrotic material. This abscess varied from 0.5 to 1.5 cm. in diameter. Both of these abscesses extended inwards and communicated with the left lateral ventricle. Nearly the whole of the surface of this ventricle was covered with a thick layer of pus and the wall over a large surface was necrotic. The lenticular nucleus of the left side contained a number of small smooth-walled gas-cysts or cavities varying from 1 to 5 mm. in diameter. In the internal capsule there were several similar gas-cysts. The right lateral ventricle, the right cerebral hemisphere, the cerebellum and the pons and medulla showed nothing abnormal on section.

Spinal Cord.—The dura mater was moderately hyperæmic. The vessels of the pia-arachnoid were hyperæmic and contained small gas bubbles. In the membranes there were gas-cysts from 1 to 3 mm. in diameter. The cord was of ordinary consistence and appeared normal.

Bacteriological Examination.—Coverslip preparations made from the lungs, heart, venæ cavæ, portal vein, pelvic veins, liver, the cerebral and spinal exudations, and the brain abscesses, showed in great numbers and in pure culture a large stout bacillus often in pairs, threes and fours end to end, and usually with capsules. Careful study of the meningeal exudate failed to demonstrate the presence of any other bacteria. Half a cubic centimeter of this pus was injected into the ear-vein of a rabbit. The animal was killed a few minutes later and put in the incubator. After five hours the animal was enormously swollen, its subcutaneous tissues being emphysematous. At the autopsy gas was found in the heart and blood-vessels and in all the organs. Capsulated bacilli similar to those injected were found in pure culture in the various organs.

At the autopsy plate and slant cultures were made on glucose agar and upon slanted coagulated blood serum from the brain abscesses, the meningeal exudate, the heart's blood, and from the liver, lungs, spleen, kidneys and portal vein, were grown both aerobically and anaerobically (Novy's jars).

The aerobic cultures were sterile after three days in the incubator. All the anaerobic cultures showed, after 24 hours in the incubator, numbers of grayish-white colonies, which after a few days were from 2 to 3 millimeters in diameter. In gelatine cultures slow liquefaction of the medium occurred. Milk was coagulated in forty-eight hours. There was slight visible growth with gas formation on potato. Sugar bouillon was rendered diffusely cloudy. The organism was non-motile. In blood serum-cultures spores were found.

The bacillus produced gas in media containing fermentable substances. Cultures of this bacillus were pathogenic for guinea-pigs and pigeons. Rabbits killed after intravenous inoculation and kept in a warm place always showed marked emphysematous swelling with typical "Schaumorgane." This bacillus stained well with the aniline stains and by Gram's staining method.

From the brain abscess and the meningeal exudate, then, as well as from the various organs there was obtained in pure culture a bacillus identical with the bacillus aerogenes capsulatus (Welch).

Microscopical Examination of the Organs.

The brain and spinal cord were hardened in 10% formalin, and portions of the other organs were hardened in Zenker's fluid and in 95% alcohol.

Central Nervous System.—Sections made from the cerebral and cerebellar cortex, from the pons and medulla and from the spinal cord, and from the brain abscesses were stained in hæmatoxylin and eosin, in eosin and methylene-blue, in thionin, and in carmine followed by Weigert's fibrin stain. A study of the meningeal changes showed marked dilatation of the blood-vessels. Many of the small arteries were filled with both polymorphous and mononuclear leucocytes. In some vessels the endothelium was partially or totally desquamated and the sub-endothelial tissue infiltrated with cells, and well marked thrombosis was found in some arteries. In some vessels both polymorphous and mononuclear leucocytes could be seen in the media and adventitia. In some places there was proliferation of the cells of the adventitia with the formation of large round or spindle-shaped cells. Only a few bacilli were seen in the vessels, but in places numbers were found in the adventitia. The exudation varied very much in thickness, being thickest at the base of the brain over the cerebellum, the pons and the medulla. The most numerous cells were polymorphous nuclear neutrophiles. Besides these there were many mononuclear cells of varying size and answering to the description of plasma cells. In addition to these in some places large round or oval mononuclear cells of the connective-tissue type were seen. Here and there a few red-blood cells were found. In some places the exudation was rich in fibrin, while in others this was scanty.

In many places on the cerebral and cerebellar cortex, proceeding along the course of the vessels in the *sulci*, there was a marked infiltration with polymorphous nuclear leucocytes and plasma cells. The exudation was, in general, rich in fibrin. The blood-vessels were dilated, and many of the arteries showed the same changes described in the meningeal vessels. In these areas bacilli were always found. In some of these broad bands of cellular infiltration in the cerebellum gas-cysts of varying size containing bacilli were seen.

Sections of the cord made at different levels showed well-marked meningitis. The exudation was most marked in the cervical and upper dorsal regions, and was in every way similar to that described in the cerebral meninges. At various places, especially, however, in the exudation over the medulla and the cervical cord, there were a number of gas-cysts. The gas-cysts of the spinal meninges varied from twenty μ to four to five mm. in diameter. The cysts of the pons and medulla did not exceed one hundred μ in diameter. These cysts were round or oval in outline and contained, both in their cavities

and along their margins, a number of large bacilli. The exudate in the neighborhood of the cysts was usually compressed.

Brain.—Sections made through the abscesses in the supramarginal and ascending parietal convolutions and including the intra-parietal tissue, and through the abscess of the superior tempero-sphenoidal convolution showed large central areas of necrotic material. This material was homogeneous and hyaline in appearance and stained diffusely with eosin. Here and there a few nuclei could be made out. Nuclear fragments were numerous in some places. In this material myriads of bacilli were found. The bacilli occurred singly and in small and large groups. About the necrotic area there was always a deep zone of dense cellular infiltration. The most numerous cells were polymorphous nuclear leucocytes. Lymphocytes and plasma cells were found in great numbers. Many of the cells resembling plasma cells contained two nuclei and were evidently proliferating. In some places cells with kidney-shaped nuclei were seen. This zone of cellular infiltration varied from one to three or four mm. in thickness. Bacilli in small and large groups, sometimes in huge clumps, could always be found in this zone. Infrequently bacilli were found in leucocytes. The blood-vessels near this zone were dilated. In many of the arteries among the red-blood cells many polymorphous nuclear and large mononuclear cells were seen. In some vessels thrombi were found. In these the intima cells were often desquamated and leucocytes were seen in the media. Well-marked cellular infiltration was found about many of the arteries. Bacilli were but rarely seen inside the vessels. Near the zone of cellular infiltration a varying number of bacilli were sometimes noticed. In rare instances in this region small spaces (gas-cysts), varying from ten to thirty μ in diameter and containing bacilli, were found.

In sections including the wall of the left lateral ventricle no trace of the ependyma remained. The ventricular surface of the sections was covered with a thick layer of hyaline material staining diffusely with eosin. This hyaline, homogeneous layer varied in thickness, and was similar in appearance to the necrotic material of the abscesses of the cortex. This layer contained myriads of bacilli and often nuclear fragments, with an occasional polymorphous nuclear leucocyte. Beneath this layer there was a thick zone of cellular infiltration in every way similar to that described in the abscesses. Many bacilli were seen among the cells in this zone. The underlying tissue showed areas of infiltration with cells about the blood-vessels, many of which contained thrombi. With the exception of the gas-cysts and the inflammatory lesions above described, no special changes were made out in the white or gray matter of the brain or cord.

Sections of the gas-cysts or cavities in the internal capsule and in the lenticular nucleus showed simply separation and compression of the tissues due to the pressure exerted by the gas. None of the cysts appeared to be dilated blood-vessels. Large numbers of bacilli were always found along the walls of the cysts. In some places large clumps or colonies were to be seen. There was no inflammatory reaction about the cysts.

Four varieties of gas-cysts could be recognized in the central nervous system in this case. (1) Cysts developed in the meningeal exudation on the surface of the cerebrum, cerebellum, pons, medulla and spinal cord. These cysts varied from twenty μ to from two to five mm. in diameter. (2) Small cysts, never exceeding fifty μ in diameter, occurring in the inflammatory exudation following the course of the arteries in the cerebellum. (3) Small cysts from ten to twenty μ in diameter, occurring near the abscesses in the parietal lobes. (4) Cysts varying from 0.5 to 1.5 mm. in diameter found in the superior tempero-sphenoidal lobe, in the lenticular nucleus and internal capsule on the left side.

Lungs.—Sections of the lungs showed slight chronic interstitial pneumonia and emphysema. There was marked congestion of the air vesicles about some of the small bronchi. No bacilli were seen in the alveoli or in the blood-vessels, though some of the latter contained many leucocytes.

Liver.—The liver showed extensive fatty degeneration, best marked in the liver cells at the periphery of the lobules. The interlobular fibrous tissue was increased, and in many places was infiltrated with cells resembling lymphocytes and plasma cells. Nuclear figures were occasionally seen in the latter cells. The veins and capillaries were congested and in many bacilli were seen. In a number of sections there were areas varying from 0.5 to 1 mm. in diameter, in which the nuclei of the liver cells did not stain. The cytoplasm was swollen and more granular than ordinarily. Many cells contained fat drops. Many of the liver cells, especially in the centre of the areas, were shrunken to one-half their normal size. In these areas the endothelial cells of the capillary walls did not stain. Occasionally leucocytes still retaining their staining properties were seen. Long stout bacilli were always found, sometimes in small, but usually in great, numbers. Small gas-cysts containing bacilli were occasionally seen. The necrotic areas bore no special relation to the central veins, the portal veins or the bile-ducts. The latter were normal. The liver tissue in general was well preserved and stained well with the usual dyes.

Spleen.—The spleen showed marked congestion, but no areas of cell destruction and no gas-cysts.

Kidneys.—The kidneys showed cloudy swelling of the epithelium of the convoluted tubules, congestion of the glomerular and intralobular capillaries, and of the veins. No bacilli and no gas cavities were found. The heart showed nothing of interest.

The bacilli noted in the sections of the various organs were identical. They were most numerous in the brain abscesses and in the meningeal exudation. The bacilli varied considerably in size. They were sometimes two μ long, but the most common forms were from four to six μ in length. A few bacilli were seven μ long. Some of the bacilli had square ends, but usually the ends were rounded. They often occurred in pairs, threes and fours, end to end. Not infrequently they were bent or curved, and some were wavy in outline. The bacilli stained well and uniformly with hæmatoxylin, thionin, methylene-blue and by Weigert's method. The last method gave the most clear-cut pictures. With this stain the outlines of the bacilli were often somewhat irregular, due to irregular swelling or contraction of their protoplasm. Slightly clubbed forms were sometimes seen. No stained capsules

were found in the tissues, but occasionally ill-defined masses resembling empty capsules were seen. Careful search of the affected tissues failed to disclose the presence of any other bacteria.

In this case it is evident that the tissue necrosis, the inflammatory lesions and the gas-cysts were due to infection by the bacillus aerogenes capsulatus. The pyogenic properties of this bacillus are now well known.

In my opinion the presence of the bacilli in such great numbers in the nervous system and their relative paucity in the blood-vessels and other organs precludes the idea that they were post-mortem invaders. When an unusual organism is found in association with inflammatory lesions it is no longer thought necessary to assume that the pyogenic cocci have caused the lesions and died out before the case came to bacteriological examination, thus reducing an organism found in large numbers and in pure culture to the level of an accidental and innocuous invader. The complete revolution of our views concerning the pyogenic properties of the typhoid bacillus is an illustration in point. The formation of gas-cysts in the brain, the cerebro-spinal exudation, and in the liver is probably to be regarded as a post-mortem change. The perineal wound must be regarded as the portal of entry for the bacilli. A search of the literature fails to disclose a case of abscess of the brain with cerebro-spinal meningitis due to the bacillus aerogenes capsulatus. I have found this bacillus in the blood-vessels of the brain in several cases without inflammatory lesions. Through the courtesy of Dr. Reuling, I have examined a section through a gas-cyst of the brain of the case he reports in this number of the Bulletin. In every respect it agrees in appearance with gas-cysts of the internal capsule and lenticular nucleus of my case.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

Resistance to Quinine of Certain Forms of Malaria.—Dr. Camac.

The value of the following temperature records is both diagnostic and therapeutic. Where the aid of the microscope is not to be had the temperature chart may be all the physician has to guide him in both diagnosis and treatment. It is with the object of drawing conclusion on these two heads that the present malarial temperature charts are exhibited. In each of the following cases the malarial parasite was, of course, found and its type determined, so that the conclusions are reliable as referring to malaria only.

Case I.—J. B. Type Æstivo-Autumnal. *Blood Examination by Dr. Hamburger.* Sept. 30 (day of admission), intracellular hyaline amœboid ring-shaped bodies; one crescent. Oct. 1, a crescent; organisms scarce; hyaline intracellular body. Oct. 2, 10 a. m., quinine gr. x; 12 m., quinine gr. v q, 4h.; p. m., one intracellular hyaline body. Oct. 3, No organisms.

Temperature.—Daily paroxysm; *not reaching normal* during the intervals; temp. normal on Oct. 4.

Treatment.—70 grains of quinine required to control fever. Time required, 3 days.

Case II.—R. B. (colored). Type Æstivo-Autumnal. *Blood examination by Dr. Pancoast.* Sept. 24 (day of admission), 7 p. m., one ring-shaped body. Sept. 25, 10 a. m., ring-shaped amœboid body. 12 m. quin. gr. x; 4 p. m., quin. gr. v. q. 4 h.

Temperature.—Daily parox.; slight drops, *not reaching the normal* (Widal's agglutination negative); temp. normal 27th.

Treatment.—95 grs. required to control fever—3 days.

Case III.—M. J. Type Æstivo-Autumnal? *Blood examination by Dr. Pancoast.* Sept. 27 (day of admission), one ring-shaped body; 10 p. m., quinine gr. x; 12 m., quinine gr. vq. 4 h.

Temperature.—Daily paroxysms; *not reaching normal during intervals.* 2 p. m., 27th, temp. 104.2; fever apparently controlled by quin.; parox. only delayed. 10 p. m., 29th, temp. 101.8. 10 p. m., 30th, temp. normal.

Treatment.—105 grs. required to control fever; time required, 3 days. Especially instructive case as blood examination was not conclusive.

Case IV.—P. C. Type Double Tertian. *Blood examination by Dr. Hunner.* Numerous organisms. 2 sets, 1st full grown in very pale corps; fine, actively motile pigment; 2d, half-grown intracellular pigment, motile; corps somewhat enlarged.

Temperature.—Parox. 27th, from 2 p. m. to 3 p. m. Parox. 28th, 2 p. m. Quin. gr. xx, 2 p. m.; quin. gr. v, 6 p. m. q. 4 h.

Treatment.—50 grains controlled fever, inclusive of time when parox. should have occurred. Time required, ½ day.

Case V.—J. S. Type Double Tertian. *Blood examination by Dr. Hunner.* Two sets of organisms: 1st group, Sept. 13, parox. 2 p. m.; 2d group, Sept. 14, parox. 6 p. m.; 1st group, Sept. 15, parox. 2 p. m.; 2d group, Sept. 16, parox. 4 p. m.

Treatment.—Sept. 16, 4 p. m., subcutaneous inject. quin. gr. xviii. Sept. 17, parox. of 1st set delayed to 6 p. m.; also modified Sept. 15, 104.8; Sept. 17, 102.6. Sept. 17, 6 p. m., intravenous inject. gr. vii ss. Sept. 17, abortive rise at 10 p. m. Sept. 18, fever controlled. Fever controlled by 25½ grs. Time required, 2 days.

Case VI.—J. B. Type Double Quartan. *Blood examination by Dr. Cushing.* Two sets of quartan parasites. Case developed on surgical side. Further blood examination made by Dr. Thayer. Oct. 26, 10 p. m., paroxysms complete; quin. grs. v, 2 and 4 p. m. Oct. 28, 2 a. m., paroxysms complete. Oct. 29, 12 noon, quin. grs. v q. 4h. Oct. 30, slight parox. Oct. 31, slight parox.

Treatment.—30 grs. greatly modified parox. of two group; 75 grs. controlled fever.

There are to be observed in these six cases several striking features: 1st, The marked resistance to quinine of the æstivo-autumnal type. 2d, The tendency of the æstivo-autumnal not to reach normal during the intervals. 3d, No form resisting the quinine beyond 3 days.

The most effectual time to exhibit quinine has been fully investigated by Golgi; Marchiafava and Bignami, and Case VI of the present series demonstrates well Golgi's observations. He finds that quinine administered in quartan fever, 4 or 5 hours (even in small doses) before segmentation readily kills the young forms, but has no influence upon the adult forms, the following paroxysms occurring uninterruptedly. The tertian, however, is readily influenced by the administration of quinine just before the paroxysms (Case IV), the following paroxysms being prevented or delayed. From the teachings of Marchiafava and Bignami the following may be concluded for tertian and quartan fever:

Full dose at crisis:	1. Parox. prevented. 2. Aborted. 3. Delayed 6-24 hours.
Full dose 6 hours before crisis:	1. Delayed. 2. Aborted. 3. Pseudocrisis.

By watching the chart and observing first its character uninfluenced by quinine, then its character after the administration of quinine, and noting at the same time when the quinine was administered with reference to the paroxysm, the diagnosis not only of malaria but of its type may sometimes be made. Fever which shows no signs of breaking three days after the administration of full doses of quinine every four hours is other than malaria; if it yields earlier than the third day, on moderate doses, it is likely to be of the tertian or quartan type, whether double or single. The tendency of the æstivo-autumnal fever to resist quinine has led the Italian observers to speak of the gradual destruction of the parasite as one of "fractional sterilization," and this tendency would induce the careful physician to prolong his quinine for a greater period in dealing with this form. Here, however, we may take as a guide the fact that the æstivo-autumnal fever often fails to touch normal during the intervals between paroxysms, whereas the tertian and quartan more commonly do. To those cases therefore who bear quinine badly it may be discontinued earlier and with greater safety in the tertian and quartan than in the æstivo-autumnal.

It may, however, with profit, be repeated, and repeated emphatically, that fever which does not show signs of *breaking* within three days, when properly met by quinine, is other than malarial, and quinine is being given not only to no advantage, but in many cases with harmful effects.

We have, therefore, in the proper observation of the temperature chart, both a diagnostic and therapeutic guide, though we have not the aid of the microscope.

It may be interesting in this connection to mention a recent conversation with Dr. John T. Metcalfe, one of Louis' students, who remembers the pre-quinine days. I think it was about 1820 that quinine was separated by Pelletier, prior to which Peruvian bark was used exclusively. The preparation known as Peruvian paste was so thick that it could be just swallowed. A tablespoonful was taken at a dose, and frequently vomiting was so severe as to require the use of opium. A 3-ounce bottle of quinine was brought to Natchez, Miss., and was sold for $90.

A New Method of Staining Malarial Parasites.—Dr. Futcher.

As Dr. Lazear and myself, during the past winter, came across a convenient method of staining malarial parasites in dry specimens, I thought it might be of interest to report it to the society. We do not claim originality, either for the method of fixing, or the method of staining, the organisms, but, so far as the combining of the two methods is concerned, we think it has not been done before. It is a very quick process and very serviceable in cases where one is called out to see a suspicious case and has not a microscope at hand with which to examine the fresh blood.

The dried-blood specimens, made in the usual way described by Ehrlich, are then fixed in a ¼ per cent. solution of formalin in 95 per cent. alcohol. It is important that the formalin solution should be made up fresh each time it is used. We have found satisfactory results by adding four or five drops of a ten per cent. aqueous solution of formalin to 10 cc. of 95 per cent. alcohol just before using. This method was first described by Benario in the Deutsche Medicinische Wochenschr., No. 27, 1894. He used a 1 per cent. solution of formalin in 90 per cent. alcohol, however. He stated that not only was the hæmoglobin of the red cells well preserved, but the granules and nuclei of the leucocytes were well fixed and took the stain particularly well. The cells were especially well stained with eosin and hæmatoxylin. The specimens are fixed in this solution for only one minute, washed in water, blotted and then stained in the special mixture.

As to the staining agent, our attention was first drawn to the use of thionin by Dr. W. G. McCallum, who referred us to an article by E. Marchoux, in the Annales de l'Institut Pasteur, Vol. ii, p. 640, 1897, in which the author gives a report on the malarial fevers of Senegal, and in which he describes his method of using thionin in staining the parasites. The author considered it especially serviceable for staining malarial organisms, but instead of formalin he used the ordinary alcohol and ether fixing method and, so far as we know, the use of formalin and this stain have not been combined before. He makes a saturated solution of thionin in 50 per cent. alcohol, of which 20 cc. are added to 100 cc. of a 2 per cent. carbolic acid solution. This solution can be kept in stock and used as required. It is perhaps better to keep the stain for some time before using as it improves with age. Thionin phenate is formed, which is believed to be the active staining agent. Only 10 to 15 seconds are required for staining.

The malarial parasites come out very distinctly as reddish-violet bodies with this stain, and it is especially serviceable in staining the ring-shaped bodies of the æstivo-autumnal infection. These are very hard to distinguish in fresh specimens and usually do not stain satisfactorily with eosin and methylene-blue. Any one who has stained specimens in this way knows how he has regretted, on examining them two or three months later, to find that they have faded. With the thionin stain the parasites retain the color much better than they do when stained with methylene-blue.

The method of fixing and staining malarial parasites is then as follows:

Make the ordinary smear preparation, fix in the formalin solution for one minute, wash in water, thoroughly dry, stain with the thionin solution for from ten to fifteen seconds; ten will probably give the most satisfactory results. Wash off the excess of stain, blot, mount in balsam and the specimen is ready to be examined. The whole operation does not last more than two minutes from the time you begin to fix until it is ready for examination, whereas with the old method of fixing with alcohol and ether, one usually has to wait two hours to get satisfactory results, and even then it is often found, if eosin and methylene-blue have been used, that the hæmoglobin of the red cells has not been properly fixed and the cells show peculiar vacuolic areas. With the formalin fixing and thionin staining the protoplasm of the reds is well fixed and practically unstained, and the parasites stand out

distinctly as reddish-violet bodies in the substance of the red cell. The ring-shaped bodies of the æstivo-autumnal variety come out much better than with any other agent in use.

We also used the thionin stain to try and bring out the flagellated processes in the æstivo-autumnal infection. Probably one of the most convenient methods for obtaining permanent preparations of the flagella is that described by Sakharov, in which an ordinary specimen on the slide is made and at the same time several specimens of blood are taken on coverslips, leaving the latter in contact with each other in a moist chamber and watching the ordinary preparation under the microscope until flagellation begins, when the coverslips in the moist chamber are taken out and drawn apart and dried. One will then most likely catch the organisms in the flagellating stage. We have fixed some of these by heat and then stained with thionin, and have obtained some good specimens showing the flagellate processes coming off from the body of the parasite. At this time we had not been using the formalin fixing, but there is no reason why it should not be substituted for the heat.

This method of fixing and staining is not to supersede the examination of the specimen of fresh blood, always the most satisfactory method, but only where staining is the only resource and rapid results are desired. We have placed under the microscope on the table specimens of the three types of malarial organism stained by this method.

Dr. Flexner.—There is a method, you will remember, which was worked out by Dr. Mallory for staining the amœba coli. The specimen is stained in thionin and placed in a weak solution of oxalic acid to remove the coloring matter from all other cells except the amœbæ. I also had the opportunity of studying recently some specimens of amœbic dysentery stained by Dr. Harris of Philadelphia, with toluidin blue and the organisms are as easily made out as when stained with thionin. I do not know whether these methods would succeed with the malarial parasite, but they might be tried.

Dr. Lazear.—During the summer I tried the toluidin blue for the malarial parasite. It is fully as good as methylene-blue, but does not stain so deeply as the thionin.

Dr. Thayer.—It appears to me that the method of staining advised by Dr. Futcher is one which is of very considerable practical value. It is often impossible for the busy practitioner to examine the fresh specimen of blood, and most of the other methods of preparation are rather delicate proceedings, at least if one wishes to obtain really good specimens. A thoroughly satisfactory method which can be carried out almost inside of two minutes is a great advance.

I should like to emphasize particularly its value in staining the æstivo-autumnal parasites. The hyaline bodies take up all dyes very feebly, and it is often extremely difficult for the unskilled eye to distinguish them. By Dr. Futcher's method of staining with thionin, however, a perfectly satisfactory specimen may instantly be obtained. I know of no method which brings out the æstivo-autumnal parasite so well.

Laparotomy for Intestinal Perforation in Typhoid Fever.—[See Bulletin for November Discussion, 1898.]

Dr. Thayer.—I had the good fortune to observe the first case which Dr. Cushing has mentioned throughout the greater part of its course. I happened to walk into the ward on the night upon which the second operation was done and found the boy in a condition of profound collapse. This had come on very suddenly, Dr. Cushing having seen the child but a short time before. When I saw him he had been vomiting; the skin was cool; there was profuse sweating; the temperature had fallen several degrees; there was abdominal tenderness; the pulse was feeble and rapid; the face was drawn; the cheeks and eyes sunken. There could scarcely have been a more typical picture of acute peritonitis. And yet, when the abdomen was opened, there was not only no peritonitis, but there was not enough disturbance to suggest the existence of obstruction to any one present. Such a picture is an excellent demonstration of the difficulties which may stand in the way of a correct diagnosis in these cases.

What Dr. Cushing has said of the leucocytes is, it seems to me, of considerable importance. I have no doubt that it is quite true that in an individual with distinct evidences of perforative peritonitis a normal or subnormal number of leucocytes is a very bad prognostic sign. I remember one or two instances of general streptococcus septicæmia where the leucocytes were normal or subnormal in number; one case in particular where there were but 3000 leucocytes to the cubic millimeter. As long ago as 1892, Werigo showed that after inoculating animals with cultures of pyogenic bacteria there occurs primarily a reduction in the number of leucocytes to the cubic millimeter. In the milder cases this initial fall is followed by a subsequent leucocytosis. In the particularly malignant and rapidly fatal cases, however, no subsequent rise in the number of leucocytes occurs. The same condition has been noted experimentally by various other observers. And I am inclined to believe that, as in pneumonia, so in other malignant general infections, a subnormal number of leucocytes may be regarded as a bad symptom, and it is not at all impossible that in Case III the fall in the number of leucocytes following the direct evidence of perforation may well have been associated with the sudden onset of what proved to be a rapidly fatal streptococcic infection, the previous leucocytosis having been due to the moderate local peritonitis about deep ulcers.

Monday, December 19, 1898.

Presentation of Pathological Specimens.—Drs. MacCallum and Harris.

Dr. MacCallum presented a case exhibiting multiple metastases from a sarcoma primary in the pelvis. The patient was a young man, aged 21, who had complained of chills and obstinate constipation with great pain on defecation. There was also severe pain in knee, hip and back, and recently considerable loss in weight and strength. Physical examination revealed signs of consolidation at left apex; tumor masses projecting laterally out of the pelvis in the inguinal regions; and per rectum a large smooth mass filling the pelvis over which the mucosa of the rectum could be

moved. There were also several subcutaneous nodules. After a very painful illness the patient developed a pleurisy and died without any great elevation of temperature.

At the autopsy the most extensive tumor growth was found in the pelvis. The pelvis was completely choked by the new growth which projected over its brim and formed the nodules palpated during life. The mass lay between the bladder and intestine, projecting into the bladder and forming a large ridge across its posterior wall. The prostate retained almost its normal appearance, the median lobe being apparently unchanged. Rectal mucosa was not involved. This large tumor was directly continuous with the chain of retroperitoneal glands which were densely matted together and surrounded the recto-vesical cul-de-sac. Sections showed that the tumor—an alveolar large round-cell sarcoma with giant cells—had invaded the bladder from without, as remains of epithelium exist over the intra-vesical projection. The prostate was almost completely replaced by the tumor mass, and the seminal vesicles pushed far back towards the rectum. Metastases occurred in the testes, liver, epicardium, lungs and mesentery, as well as the subcutaneous tissues. The lymphatic glands, with the exception of the immediately adjacent retroperitoneal glands, were very slightly involved.

In the lung, in addition to a mass at the hilum, the metastases were chiefly in the form of flat, button-like nodules on the pleural surface, and on cutting up the arteries which run to these nodules, the arterial walls were seen to be infiltrated with tumor cells so as to form a thick cord-like structure with relatively narrow lumen—a few of these arteries were actually plugged with masses of tumor cells, evidently indicating the channel of metastasis. The possibility, perhaps, cannot be excluded that the perivascular involvements in the neighborhood of the subpleural nodules are merely extensions in the lymphatics of the vessels from the tumor masses which themselves may have arisen from an infection of the pleura—an idea supported by the extensive involvement of the costal pleura.

The very similar cases of Andree and Zenker (both reported in Virchow's Archiv) were referred to.

Dr. Harris.—The greater interest of this case, no doubt, lies in the pathological statement that Dr. MacCallum has presented, but the bacteriological findings will, I think, prove by no means unworthy of consideration.

The bacteriological analysis of the autopsy was as follows: The streptococcus pyogenes was isolated in pure culture from the liver, the spleen and a sarcomatous nodule on the abdominal wall; associated with this organism was the bacillus proteus vulgaris in a culture obtained from the lung.

Subsequently, additional interest was added to the case by the accidental infection with the streptococcus of Dr. Cushing and Miss Reed. In the former, the symptoms of beginning trouble appeared within six hours at the site of a small prick in one finger; within twelve hours the axillary glands and lymphatics of the limb were swollen and tender. The symptoms of infection becoming more pronounced, surgical aid was required, and, with excision of the infected area, recovery soon set in. From the excised portion of the finger the streptococcus pyogenes was obtained in pure culture.

In the latter case of infection the trouble was entirely local in character, being confined to the tissues at the root of a finger-nail. Redness, pain, swelling and pus formation were the cardinal symptoms. The finger received surgical treatment and slowly healed by granulation. Coverslips from pus showed streptococcus. In consideration of these two cases of accidental infection it was thought advisable to continue the bacteriological study of the organism, and tests were made to determine its virulency upon mice. The first mouse received subcutaneously 0.3 cc. of a bouillon culture. It was found dead next morning, and had probably died within twelve hours—rather a rapid result. The animal was autopsied, but all that was found was a subcutaneous œdema with possibly a small focus of necrosis. The inguinal glands were swollen, but not hemorrhagic. The axillary glands were in the same condition, and all the vessels leading to them were tremendously engorged. The lumbar and mesenteric glands were increased in size. The spleen was greatly swollen, dark-red and soft; the liver was also enlarged and friable; the kidneys in the same state, but pale instead of dark. Cultures from the organs of the mouse were negative, the organism being recovered only from the site of inoculation.

From that organism the second mouse was inoculated, using only one small loopful from the agar culture and administered beneath the skin. This mouse died in sixty-five hours, and the same appearances were found on autopsy of this animal. In addition the lungs showed numerous broncho-pneumonic patches. From these and from the heart's blood the organism was obtained in abundance.

From a liver culture of this mouse a third mouse was given the same quantity, and it died in less than sixty hours.

Upon the grounds of susceptibility to infection with the streptococcus pyogenes we are at once struck by the fact that the human being is very much more prone to this infection than mice, for, in a large number of cases occurring in the human subject, the isolated organism fails to kill a mouse inoculated with it. I can call to mind several occasions where I injected rabbits and mice with streptococcus obtained from cases of puerperal septicæmia, and had entirely negative results. Therefore, upon the high degree of virulence exhibited by this streptococcus, is the bacteriological side of the case presented.

NOTES ON NEW BOOKS.

Twenty-ninth Annual Report of the Massachusetts State Board of Health. (*Boston: Wright & Potter Printing Co.*, 1898.)

The Massachusetts State Board of Health Report for 1897 contains the records of work done by the Board during the year set forth in the lucid style so long characteristic of preceding issues. A general report, including a joint report upon the restoration of Green Harbor, is followed by a section relating to water-supply and sewerage. This section contains a report to the legislature, advice to cities and towns regarding their respective water-supplies and sewerage systems, records of chemical and microscopical work done in the examination of water-supplies and rivers, water-supply statistics and a complete account of the work at the Lawrence Experiment Station on sewage purification and the filtration of

water. The sewage purification of cities and towns in Massachusetts is finally discussed.

Section 3 consists of a report on food and drug inspection and the analytical examination for adulterations, etc.

Sections 4, 5, 6 and 7 describe the work and results of the State Bacteriological Laboratory, including diagnostic examinations and the making of antitoxin.

Statistical summaries of disease and mortality follow, and a review of the sanitary statistics of the various towns of the commonwealth completes the report.

There is, perhaps, no publication in this country in which statistics are more carefully worked out, or made to yield more definite information, than those collected by the Massachusetts State Board of Health, largely due to the fact that its well-known secretary is one of the most careful and patient statisticians in this country.

From this report, we gather that infectious diseases in Massachusetts have steadily decreased during the last forty years, with the exception of a slight rise in 1896. An outbreak of small-pox, limited to about eighteen cases, occurred in Boston and neighboring municipalities during the first half of the year. In this connection, and in view of the recent retrograde changes in the vaccination laws of England, it is interesting to note that during the ten years (1888–1897) the death-rate in Massachusetts amongst vaccinated small-pox patients was 6.3 per cent., and amongst unvaccinated small-pox patients 25.5 per cent., about four times greater. We may note here that in Massachusetts, also, the vaccination laws suffered, in 1894, an unnecessary amendment, still in force, allowing any regular physician to certify to the unfitness of a child for vaccination, so exempting the child from the legal restrictions otherwise imposed. The granting of such exemptions should certainly be left to the discretion of boards of health.

Typhoid fever showed a reduction of about twelve per cent. Careful consideration of the mortality lists of the different Massachusetts towns confirms once more the rule that a continued high death-rate from this disease in any one community points to the probable pollution of the water-supply of that community and calls for careful investigation. The number of diphtheria cases steadily decreased during the years 1894, 1895 and 1896. The fatality of cases diminished in a much greater ratio due probably to improved treatment and greater sanitary precautions. It can be definitely established that the fatality of epidemics, as well as their extent, is generally lessened by rigid supervision and painstaking care.

The epidemic of cerebro-spinal meningitis, which occurred early in this year (1897), has been exhaustively treated in the monograph of Councilman, Mallory and Wright, to whom the investigation of the epidemic was entrusted by the State Board of Health. This monograph is abstracted in the report. It is interesting to compare with this epidemic of the year 1897 in Boston, the similar epidemic in Chicago during the year 1898, an account of which has been recently issued by the Chicago Health Department.

The food and drug inspection and examination upset some of the popular notions regarding the supposed extensive adulteration of foods. The adulterations in most cases are usually of a nature commercially fraudulent rather than physiologically harmful. It is curious to note that the production of pure butter is provided for by the maintenance of no less than four separate sets of officials, while on the other hand, the laws supposed to control the sale of poisons allow the unlimited sale of proprietary medicines containing violent irritating poisons or narcotics, a defect certainly requiring correction.

In most of the large cities of the State, bacteriological laboratories have been established for the diagnosis of diphtheria, tuberculosis, malaria, etc. The bacteriological laboratory of the State Board, in addition to the production of diphtheria and tetanus antitoxin, undertakes diagnostic work for those communities unprovided with a local laboratory. The use of formaldehyde as a gaseous disinfectant has become quite general throughout the State.

A large part of the report deals, as usual, with the analysis of the public water-supplies of the State, and also of rivers not now used for water-supply but receiving sewage from communities on their banks, a very provident proceeding; also with the investigations of the Lawrence Experiment Station on the filtration of water and disposal of sewage. In January, 1897, the laboratory for water analysis was transferred from the rooms of the Institute of Technology to the State House. Both this laboratory and that of the Experiment Station at Lawrence are now under the charge of Mr. H. W. Clarke. The chemical and microscopical methods developed in these laboratories continue in use. The bacteriological work is restricted to the usual efficiency tests of the filters and examination of Merrimac river water at the Experiment Station. No record of bacteriological work on the other public water-supplies is given. Owing to the distance which many of the samples of water must travel to reach the laboratory, and to the difficulty and expense of providing cold storage in transit for them, we think it probable that the additional information which may be obtained by bacteriological analysis of the water-supplies of the whole State is likely always to be restricted to qualitative work, omitting the quantitative as impracticable. Nevertheless, so many interesting and valuable chemical and biological determinations embracing not only the mere analytical results, but also the methods of analysis themselves, have come from the laboratories of the State Board in the past, that one is tempted to hope the near future may see quantitative bacteriological methods employed, for a time at least, on all the water-supplies of Massachusetts, if only to demonstrate their practicability or impracticability, in such work as the Board undertakes for the public. We think that the value of such bacteriological work is considerable and its practicability has been already amply demonstrated, certainly where the laboratory can be reached within a few hours of the collection of samples. The Lawrence experiments this year (1897) have been devoted to a continuation of the experiments of last year (1896) on the purification of tannery, paper-mill and wool-scouring establishments, on the filtration of highly polluted waters, and on the removal of iron from the waters of certain parts of the State.

Under food and drug inspection, and in addition to the ordinary routine work, the foil used for wrapping various preparations, the metal stoppers of liquid preparations, etc., have been examined for lead with interesting results. In certain countries, the inspections of these wrappers and stoppers as well as of culinary utensils, beer faucets, etc., is controlled by law. The refractometer, principally, is used in the detection of adulteration of such fats as butter, lard, olive oil, etc. A large percentage of cheap jellies were found to contain no trace of the raspberry, strawberry, etc., which the label proclaimed as present.

The report of the bacteriological laboratory of the Board at the Bussey Institute, under the charge of Dr. Theobald Smith, contains a number of tables illustrative of the results of the use of antitoxin, classification of the bacteriological diagnoses made and of the examinations for the malarial organisms.

Under the *Health of Towns*, an epitome of the reports of the various boards of health of the State is given. The action of the Lowell authorities in attaching a "poison" label to all the faucets in the mill fed with canal water shows that they at least are troubled with few doubts on the dangers of polluted water-supplies.

In conclusion, we may congratulate the State Board of Health, through its president, Dr. Walcott, on the continued excellence of its Annual Report as exemplified in this issue. It must be confessed that we miss the detailed accounts of methods of water analysis, their applications and limitations, which have made certain of the previous reports indispensable adjuncts to chemical, biological and bacteriological laboratories throughout this country. No one institution has contributed more to these subjects in the past; certainly no one of these subjects is yet exhausted. We believe that much of the information bearing on these points is still practically unknown in many sections of the country. Nor can we do other-

wise than regret that the able pen of Dr. Smith has not yielded to this report some account of the routine methods in his department. Changes in technique, however slight, are often of considerable value, and in any case, the repeated publication of even an unchanging routine, wearisome as it may seem, gradually tends to bring about a greater uniformity in method as new laboratories are established and the latest and most successful methods are considered for adoption. To the sanitarian and statistician, in general, the present volume will prove fully as interesting as its predecessors, but the student, the analyst and the ubiquitous "laboratory man" will certainly turn back, with some disappointment, to the reports of 90-96.

To the general public, the explanations accompanying some of the statistical tables of this report and the brief summaries of the conclusions to be deduced from the tables are most valuable. We can only wish that this method of making clear to "the laity" the meaning of the endless succession of figures in which statisticians delight was more extended in this report and more generally followed in others of a similar nature. H. W. H.

A Primer of Psychology and Mental Disease. For use in Training Schools for Attendants and Nurses, and for Medical Classes. By C. B. Burr, M. D., Medical Director of Oak Grove Hospital, &c. Second Edition. Thoroughly Revised. (*The F. A. Davis Co., Philadelphia, New York, Chicago*, 1898.)

The appearance of a second edition of Dr. Burr's Primer of Psychology is, in itself, evidence that it has met a want and, considering that there are other more or less similar works to compete with it in its rather limited circle of patronage, is an indication of its worth. The present edition, in addition to the general revision, has had added an address given before the Training School class of the Eastern Michigan Asylum, in 1895, a valedictory address on the occasion of his leaving that institution.

If one is to offer any criticism of the work it would be on some minor point, such, as for example, the statement that in mania there is no tendency to suicide. Maniacs do sometimes commit impulsive suicide, and like most other insane are to be considered as rather uncertain in their conduct and needing watching. This and possibly one or two other similar statements should be less absolute, and in a future edition their modification is suggested. As a treatise for the instruction of hospital attendants we can heartily recommend this book.

Archives of the Roentgen Ray. Edited by W. S. Hedley, M. D., and Sidney Rowland, M. A. Vol. II, No. 4; Vol. III, No. 1. (*W. B. Saunders, Philadelphia*, 1898.)

These two issues of this now well-known publication appear to be fully equal to their predecessors, and to contain the usual number of scientific communications. Most of them are of a rather technical character, relating to the physical characteristics of the X-Rays and their management, as would be naturally expected, but one or two are of medical interest. One of these is the preliminary notes of Drs. Wolfenden and Ross on the influence of the Roentgen Rays upon the growth and activity of bacteria and micro-organisms, in which they were found to have a very marked stimulating influence on the bacillus prodigiosus. The authors are continuing their research on the pathogenic bacilli especially, and it will be an important gain if they can give us some authoritative data on their behavior under the action of the rays.

The same issue reproduces from the *British Medical Journal* an abstract of the papers and discussions on the uses of the Roentgen Rays in the diagnosis of tuberculosis at the late congress on this disease at Paris last summer. Their value, in this particular direction, seems fairly settled, or at least highly probable, when they are utilized by experienced operators.

On Cardiac Failure and its Treatment. With special reference to the use of baths and exercises. By Alexander Morison, M. D., Edin., M. R. C. P., Ed. (*London: The Rebman Publishing Co., Ltd.*, 1897).

This work is a scientific monograph on cardiac weakness, a condition that is sometimes too little recognized, though, unfortunately frequent enough and often of serious importance, even without actual irreparable organic disease affecting the mechanical action of the heart. Whether it be the nervous system that is at fault, or the muscular tissue has lost its tone, or the heart is embarrassed by the mal-coöperation of other important organs or tissues, the general result is alike in all, a cardiac failure, varying only in degree in any particular case. The recognition and treatment of each and all of these factors is an important question, and serves to indicate how complete in this, as in other affections, the investigation of the disorder should be from the very beginning of the treatment.

The book appears to give within its compass reliable and thorough monographs of its subject, and the latter portion on the treatment of these conditions will be doubtless found valuable and suggestive. The remarks upon and descriptions of the gymnastic and hydrotherapeutic methods ought to be particularly useful as comparatively new in our literature, and the author has supplemented his own skilled observations and opinions with an appendix by Dr. Groedel, of Bad-Nauheim, who has also had the revision of the chapters on these special subjects.

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